

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A



1/60

6472179

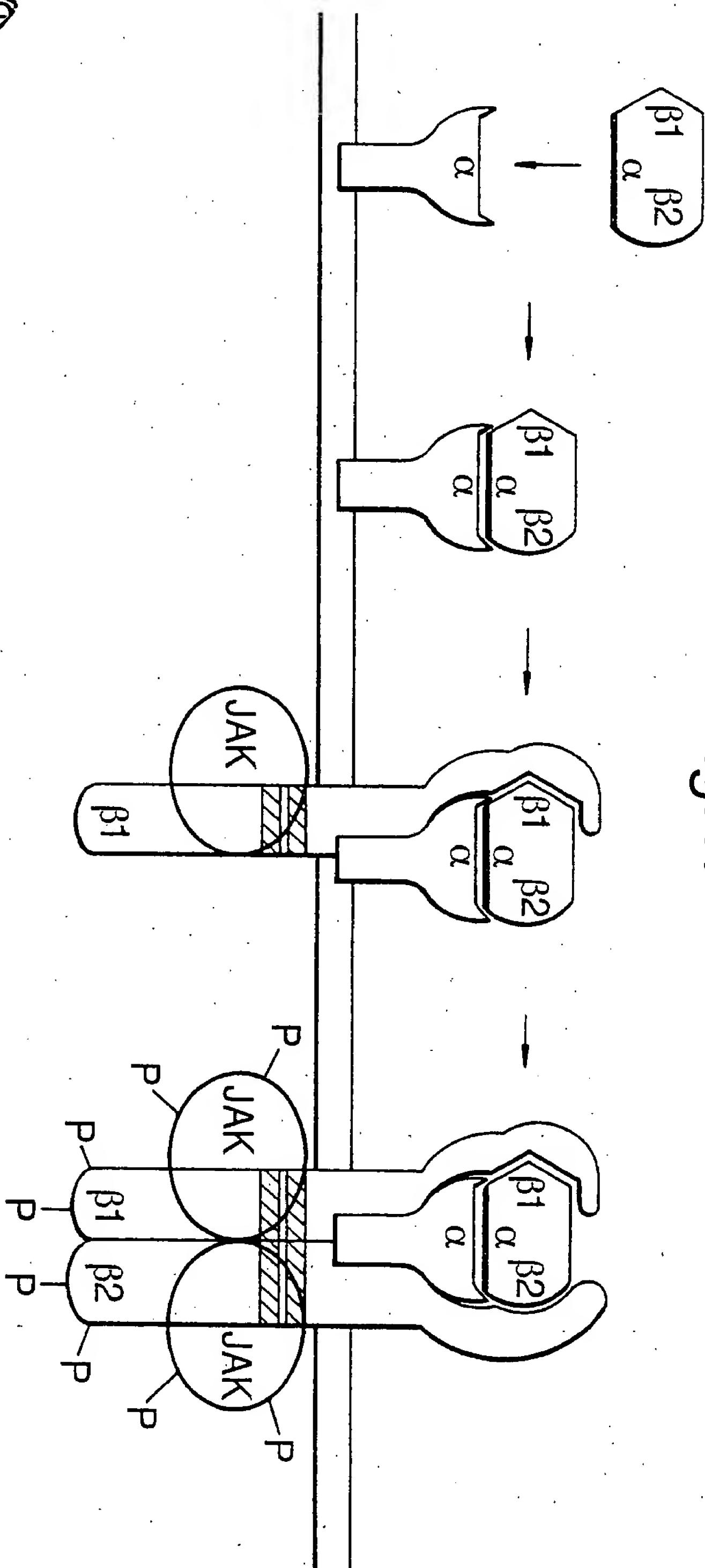


Fig. 1.



Fig.2.

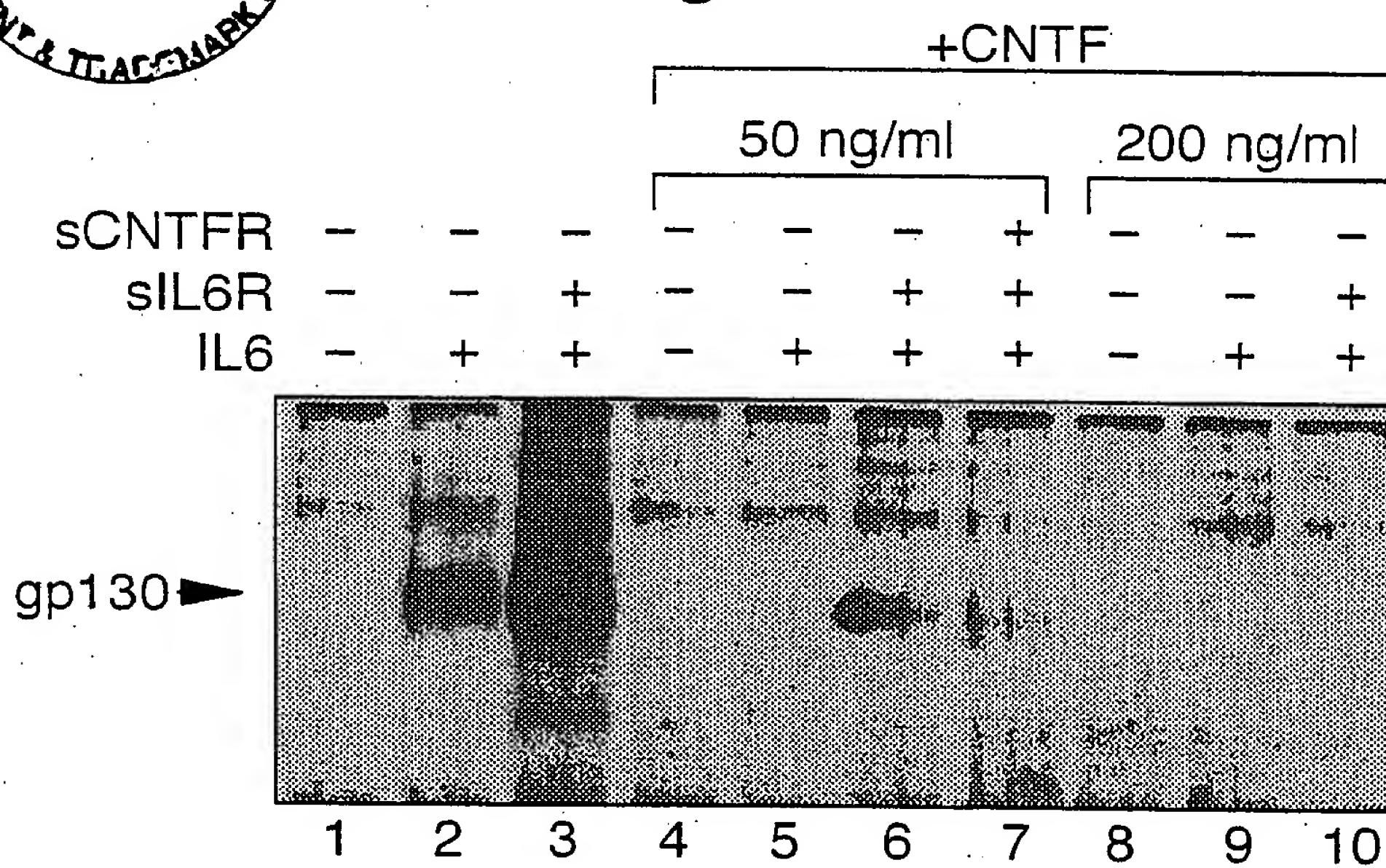
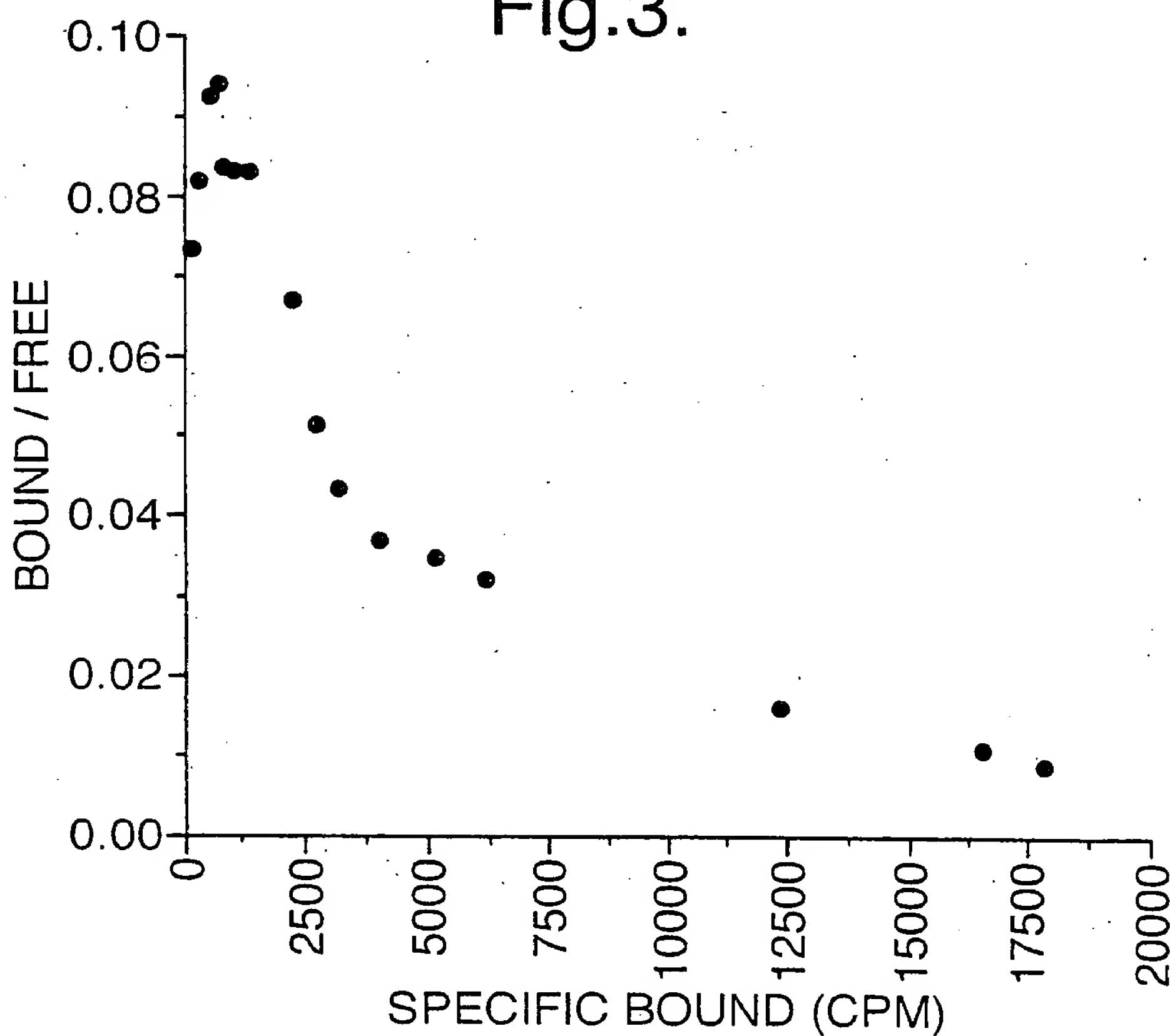


Fig.3.



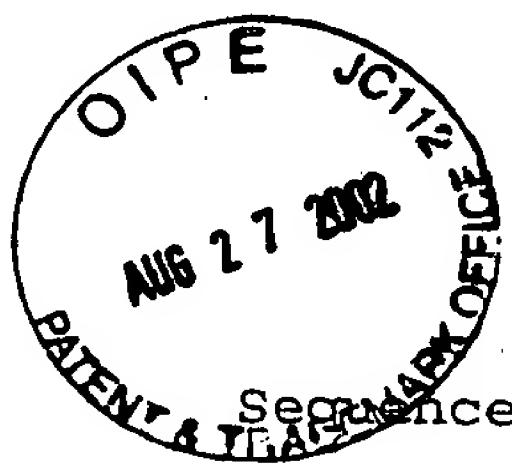


Fig. 4A

Amino acid sequence of human gp130-Fc-His6

Sequence Range: 1 to 861

10	20	30	40	50	60
*	*	*	*	*	*
MVTLQTWVVQALFIFLTTESTGELLDPCGYISPESPVVQLHSNFTAVCVLKEKCMDYFHV					
70	80	90	100	110	120
*	*	*	*	*	*
NANYIVWKTNHFTIPKEQYTIIINRTASSVTFTDIASLNIQLTCNILTFGQLEQNIVYGITI					
130	140	150	160	170	180
*	*	*	*	*	*
ISGLPPEKPKNLSCIVNEGKKMRCEWDGGRETHLETNFTLKSEWATHKFADCKAKRDTPT					
190	200	210	220	230	240
*	*	*	*	*	*
SCTVDYSTVYFVNIEVWVEAENALGKVTSVDHINFDPVYKVKPNPPHNLSVINSEELSSIL					
250	260	270	280	290	300
*	*	*	*	*	*
KLTWTNPSIKSVIILKYNIQYRTKDASTWSQIPPEDTASTRSSFTVQDLKPFTEYVFRIR					
310	320	330	340	350	360
*	*	*	*	*	*
CMKEDGKGWSDWSEEASGI TYEDRPSKAPSFWYKIDPSHTQGYRTVQLVWKTLPFEEAN					
370	380	390	400	410	420
*	*	*	*	*	*
GKILDYEVTLTRWKSHLQNYTVNATKLTVNLNDRYLATLTVRNLVGKSDAAVLTIACD					
430	440	450	460	470	480
*	*	*	*	*	*
FQATHPVMDLKAFPKDNMLWVEWTPRESVKKYILEWCVLSDKAPCITDWQQEDGTVHRT					
490	500	510	520	530	540
*	*	*	*	*	*
YLRGNALAESKCYLITVTPVYADGPGSPESIKAYLKQAPPSKGPTVRTKKVGKNEAVLEWD					
550	560	570	580	590	600
*	*	*	*	*	*
QLPVDVQNGFIRNYTIFYRTIIGNETAVNVDSSSHTEYTLSLTSDTLYMVRMAAYTDEGG					
610	620	630	640	650	660
*	*	*	*	*	*
KGPEFTFTPKFAQGEIES GEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMIS					
670	680	690	700	710	720
*	*	*	*	*	*
<u>RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEOYNSTYRVVSVLTVLHODWL</u>					
730	740	750	760	770	780
*	*	*	*	*	*

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A

4/60

Fig. 4B

NGKEYKCKVSNKALPAPIEK TISKAKGOPREPOVYTLPPS RDELTKNOVSLTCLVKGFYP

790 800 810 820 830 840

* * * * * *

SDIAVEWESNGOPENNYKTT PPVLDSGDGSFFLYSKLTVDK SRWOQGNFSCSVMHEALHN

850 860

* *

HYTOKSLSLSPGKHHHHHH.

Fig. 5.

The amino acid sequence of human IL-6R α -Fc

Sequence Range: 1 to 594

10 20 30 40 50 60

* * * * * *

MVAVGCALLAALLAAPGAAL APRRCPAQEVARGVLTSLPG DSVTLTCPGVEPEDNATVHW

70 80 90 100 110 120

* * * * * *

VLRKPAAGSHPSRWAGMGRR LLLRSVQLHDSGNYSCYRAG RPAGTVHLLVDVPPEEPQLS

130 140 150 160 170 180

* * * * * *

CFRKSPLSNVVCEWGPRTSP SLTTKAVLLVRKFQNSPAED FQEPCQYSQESQKFSCQLAV

190 200 210 220 230 240

* * * * * *

PEGDSSFYIVSMCVASSVGS KFSKTQTFQGCGILQPDPAA NITVTAVARNPRWLSVTWQD

250 260 270 280 290 300

* * * * * *

PHSWNSSFYRLRFELRYRAE RSKTFTTWMVKDLQHHCVIH DAWSGLRHVQLRAQEEFGQ

310 320 330 340 350 360

* * * * * *

GEWSEWSPEAMGTPWTESRS PPAENEVSTPMQALTINKDD DNILFRDSANATSLPVQDAG

370 380 390 400 410 420

* * * * * *

EPKSCDKTHTCPAPPELL GGPSVFLFPPPKPKDTLMISR TPEVTCVVVDVSHEDP EVKE

430 440 450 460 470 480

* * * * * *

NWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHODWLN GKEYKCKVSNKALPAPIKT

490 500 510 520 530 540

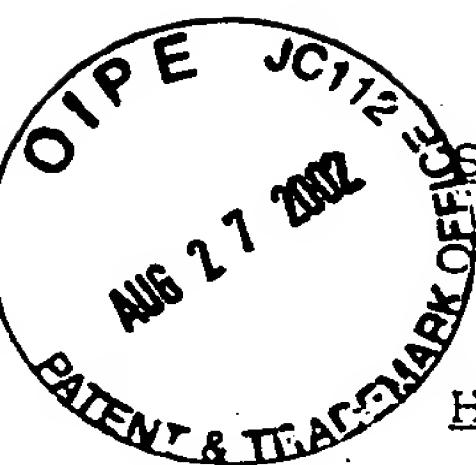
* * * * * *

ISKAKGOPREPOVYTLPPSR DELTKNOVSLTCLVKGFYPS DIAVEWESNGOPENNYKTTP

550 560 570 580 590

* * * * * *

PVLDSDGSFFLYSKLTVDKS RWOOQGNFSCSVMHEALHN YTOKSLSLSPGK.



Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A

5/60

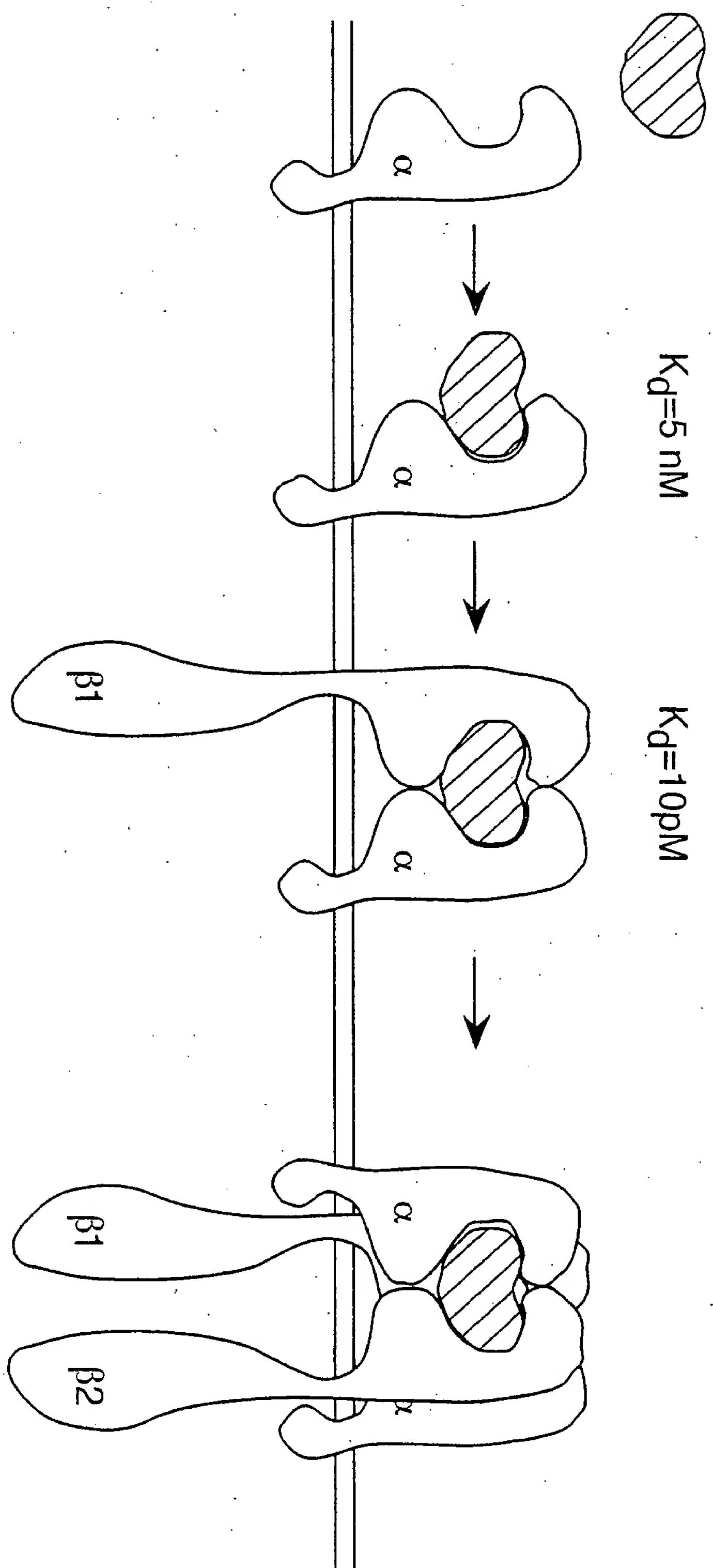
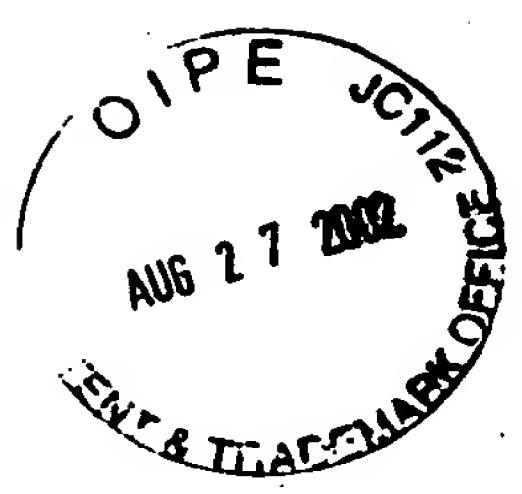


Fig. 6.

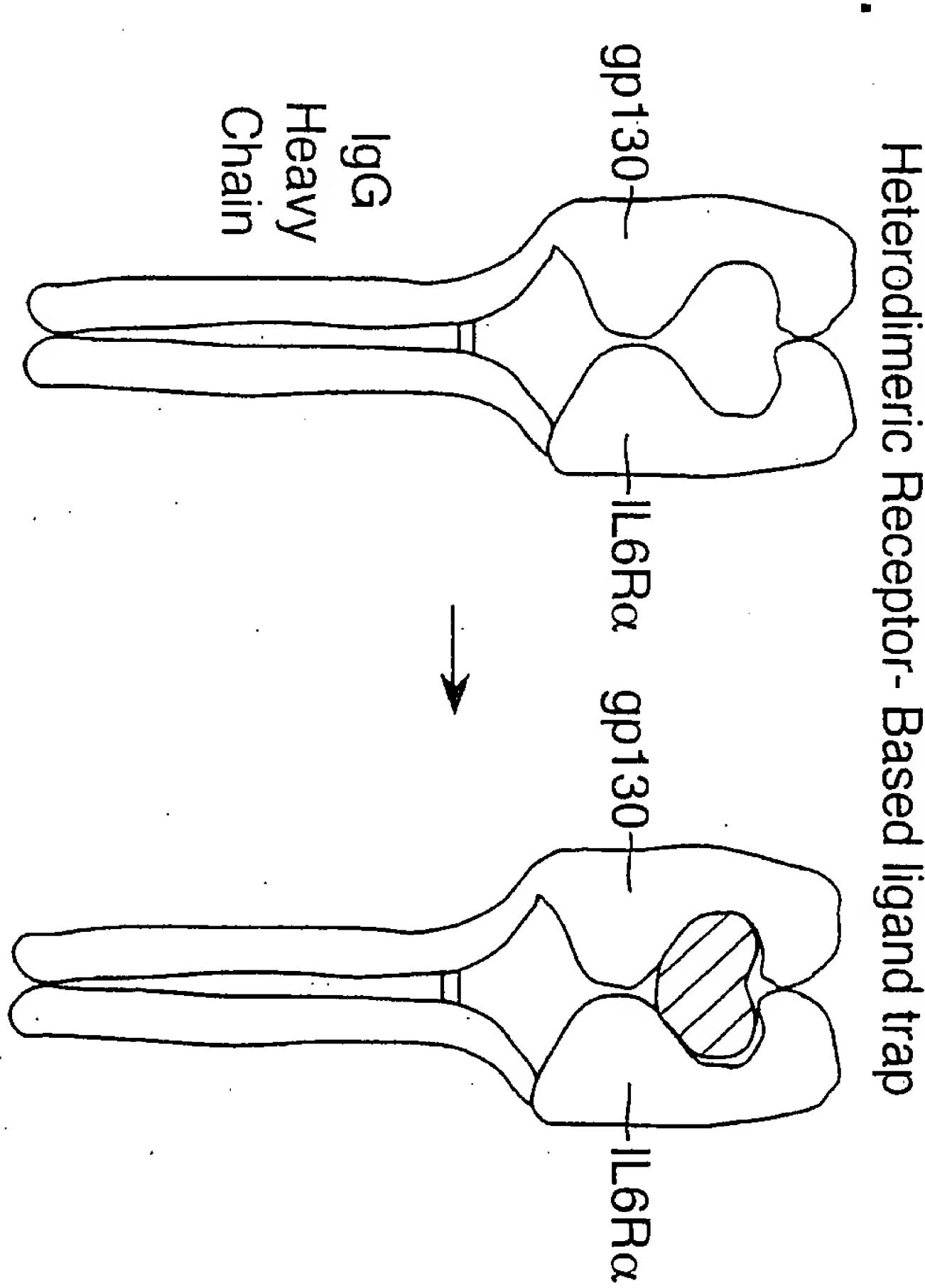
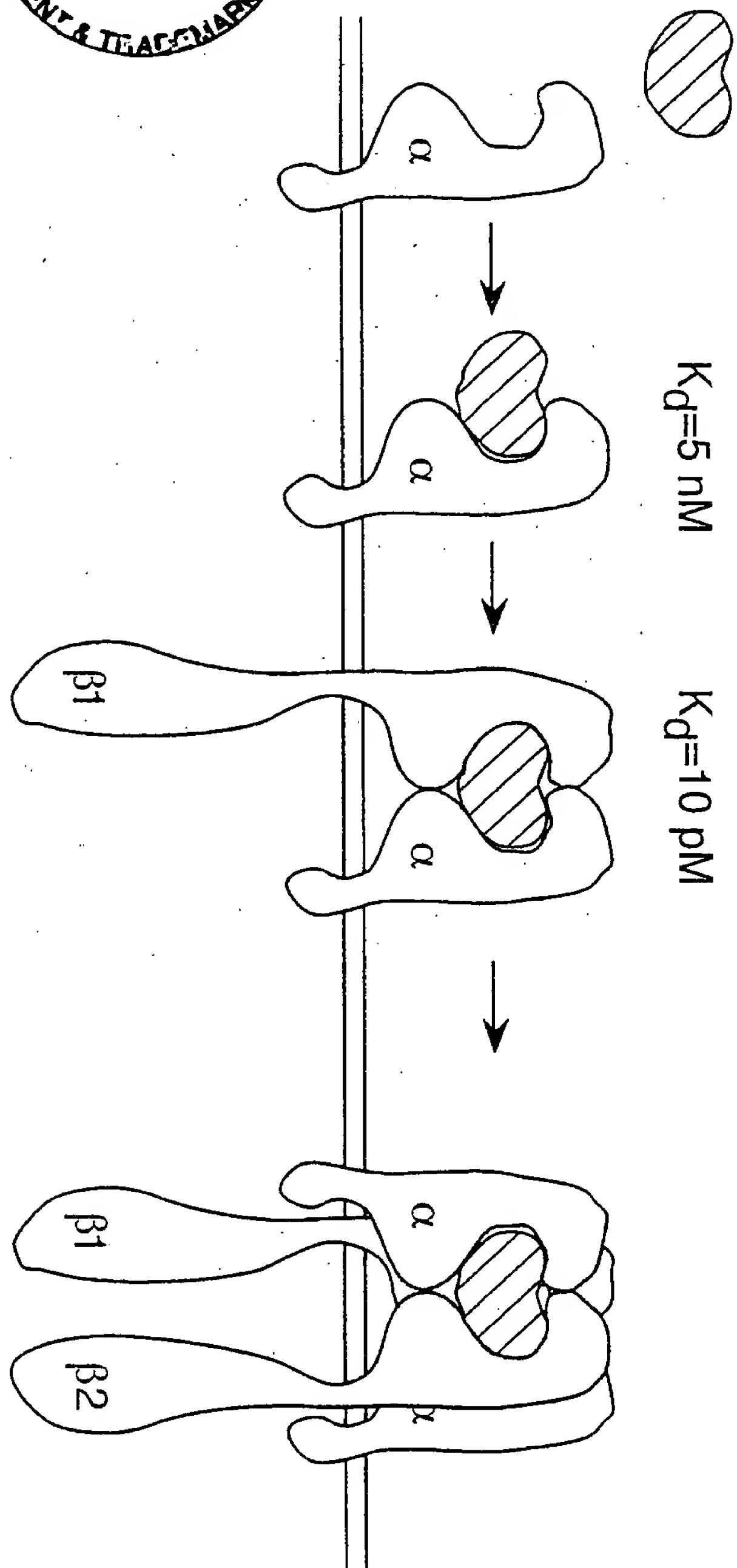


Fig. 7. Heterodimeric Receptor-Based ligand trap

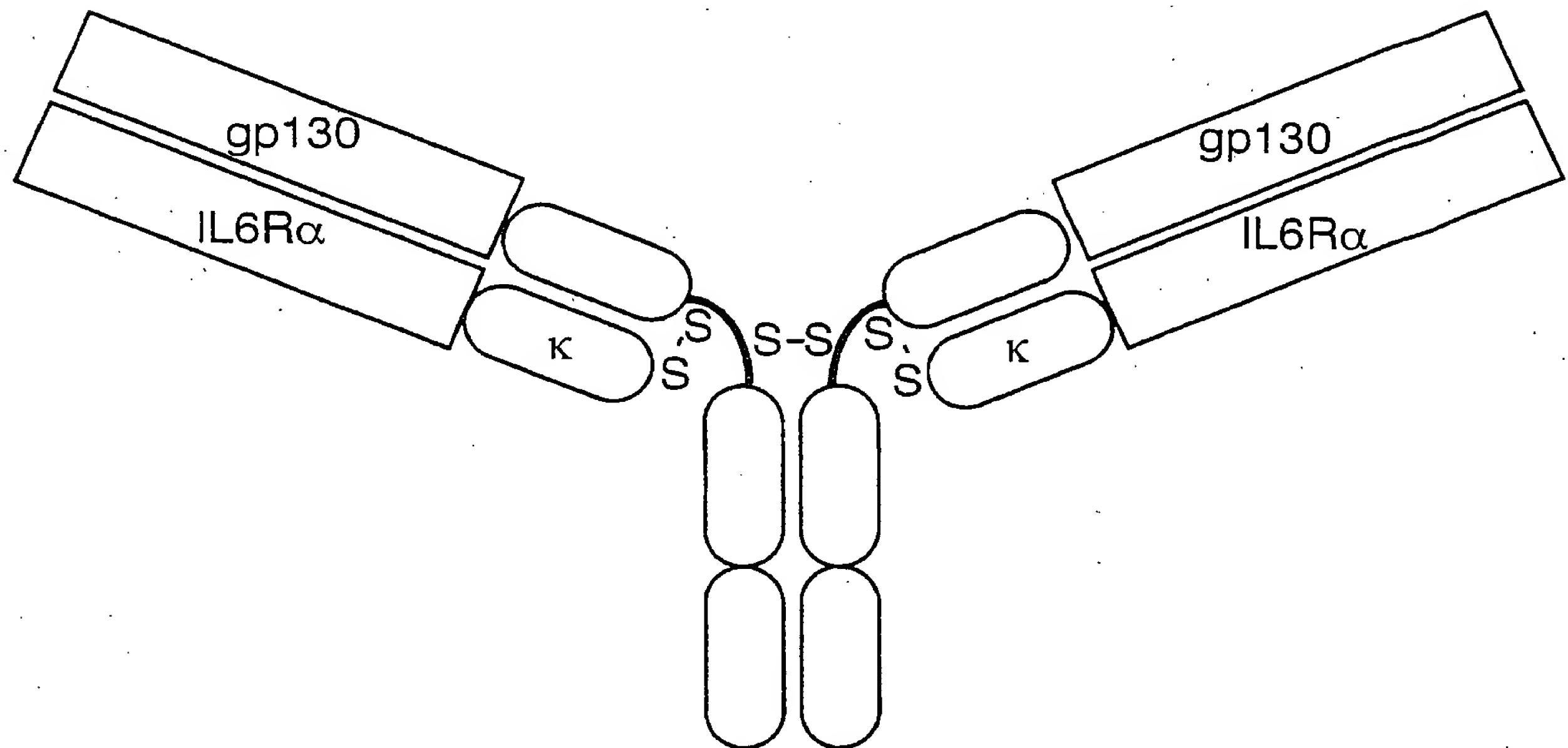
Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A

7/60

OIPE JC112
AUG 27 2002 EFC/E

Fig.8.

Immunoglobulin Heavy/Light Chain receptor Fusions



8/60

Fig. 9A

Amino acid sequence of gp130-Cγ1

Sequence Range: 1 to 952

10 20 30 40 50 60
* * * * * *
MVTLQTWVVQALFIFLTTE S TGELLDPCGYISPESPVQL HSNFTAVCVLKEKCMDYFHV

70 80 90 100 110 120
* * * * * *
NANYIVWKTNHFTIPKEQYT IINRTASSVTFTDIASLNIQ LTCNILTFGQLEQNIVYGITI

130 140 150 160 170 180
* * * * * *
ISGLPPEKPKNLSCI VNEGK KMRCEWDGGRETHLETNFTL KSEWATHKFADCKAKRDTPT

190 200 210 220 230 240
* * * * * *
SCTVDYSTVYFVNIEVWVEA ENALGKVTS DHINFDPVYKV KPNPPHNL SVINSEELSSIL

250 260 270 280 290 300
* * * * * *
KLTWTNPSIKSVIILKYNIQ YRTKDASTWSQI PPEDTAST RSSFTVQDLKPFT EYVFRIR

310 320 330 340 350 360
* * * * * *
CMKEDGKG YWSDWSEEASGI TYEDRPSKAPSFWYKIDPSH TQGYRTVQLVWKT LPPFEAN

370 380 390 400 410 420
* * * * * *
GKILDYEVTLTRWKSHLQNY TVNATKL TVNLTNDRYLATL TVRNLVGKSDAAVLTI PACD

430 440 450 460 470 480
* * * * * *
FQATHPVMDLKAFPKDNMLW VEWTTPRESVKKYILEWCVL SDKAPCITDWQQEDGT VHRT

490 500 510 520 530 540
* * * * * *
YL RGNL A ESKCYL I ITVTPVY ADGPGSPESIKAYLKQ APPS KGPTVRTKKVGKNEAVLEWD

550 560 570 580 590 600
* * * * * *
QLPV DVQNG FIRNYTIFYRT IIGNETAVNV DSSHT EYTLS SLTS DTL YMVRMAAY TDEGG

610 620 630 640 650 660
* * * * * *
KDGPEFTFTPKFAQGEIES GASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTV

670 680 690 700 710 720
* * * * * *
SWNS GALTSGVHT FPAVLOS S GLYSLSSV VTVPSSSLGTO TYICNVN HKPSNTKV DKKVE

730 740 750 760 770 780
* * * * * *

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A

9/60

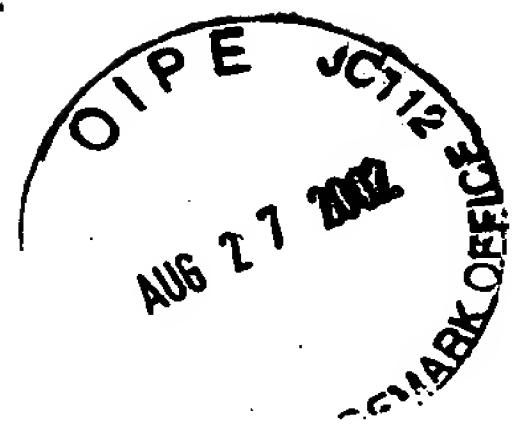


Fig. 9B

790 800 810 820 830 840
* * * * * *
WYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHODWLNG KEYKCKVSNKALPAPIEKTI
850 860 870 880 890 900
* * * * * *
SKAKGOPREPOVYTLPPSRD ELTKNOVSLTCLVKGFYPSD IAVEWESNGOPENNYKTPPP
910 920 930 940 950
* * * * *
VLDSDGSFFLYSKLTVDKSR WOOGNVFSCSVMHEALHNHY TOKSLSLSPGK*

Fig. 10.

Amino acid sequence of gp130Δ3fibro

Sequence Range: 1 to 332

10 20 30 40 50 60
* * * * * *
MVTLQTWVVQALFIFLTTE S TGELLDPCGYISPESPVQL HSNFTAVCVLKEKCMDYFHV
70 80 90 100 110 120
* * * * * *
NANYIVWKTNHFTIPKEQYT I INRTASSVTFTDIASLNIQ LTCNILTFGQLEQNRYGITI
130 140 150 160 170 180
* * * * * *
ISGLPPEKPKNLSCI VNEGK KMRCEWDGGRETHLETNFTL KSEWATHKFADCKAKRDTPT
190 200 210 220 230 240
* * * * * *
SCTVDYSTVYFVNIEVWVEA ENALGKVTS DHINFDPVYKV KPNPPHNL SVINSEELSSIL
250 260 270 280 290 300
* * * * * *
KLTWTNPSIKSVIILKYNIQ YRTKDASTWSQIPPEDTAST RSSFTVQDLKPFT EYVFRIR
310 320 330
* * *

CMKEDGKGWSDWSEEASGI TYEDRPSKAPSG



10/60

Fig.11.

Amino acid sequence of J-CH1

Sequence Range: 1 to 121

10	20	30	40	50	60
*	*	*	*	*	*
<u>SGGQGTLVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCL VKDYFPEPVTVSWNSGALT</u>					
70	80	90	100	110	120
*	*	*	*	*	*
<u>GVHTFPAVLOSSGLYSLSSV VTVPSSSLGTOTYICNVNHK PSNTKVDKKVEPKSCDKTHT*</u>					

Fig.12.

Amino acid sequence of Cy4

Sequence Range: 1 to 330

10	20	30	40	50	60
*	*	*	*	*	*
<u>SGASTKGPSVFPLAPCSRST SESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPALQ</u>					
70	80	90	100	110	120
*	*	*	*	*	*
<u>SSGLYSLSSVVTVPSSSLGT KTYTCNVDHKPSNTKVDKRV ESKYGPPCPSCPAPAEFLGGP</u>					
130	140	150	160	170	180
*	*	*	*	*	*
<u>SVFLFPPPKPKDTLMISRTPE VTCVVVDVSQEDPEVQFNWY VDGVEVHNAKTKPREEQFNS</u>					
190	200	210	220	230	240
*	*	*	*	*	*
<u>TYRVSVLTQLHQDWLNGKE YKCKVSNKGLPSSIEKTISK AKGQPREPQVYTLPPSQEEM</u>					
250	260	270	280	290	300
*	*	*	*	*	*
<u>TQNQVSLTCLVKGFYPSDIA VEWESNGQPENNYKTPPPVL DSDGSFFLYSRLTVDKSRWQ</u>					
310	320	330			
*	*	*			
<u>EGNVFSCSVMHEALHNHYTQ KSLSLSLGK*</u>					

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A



11/60

Fig.13.

Amino acid sequence of κ-domain

Sequence Range: 1 to 108

10	20	30	40	50	60
*	*	*	*	*	*
SGTVAAPSVFIFPPSDEQLK SGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQ					
70	80	90	100		
*	*	*	*		
DSKDSTYSLSSLTLSKADY EKHKVYACEVTHQGLSSPVT KSFNRGEC*					

Fig.14.

Amino acid sequence of λ-domain:

Sequence Range: 1 to 107

10	20	30	40	50	60
*	*	*	*	*	*
SGPKAAPSVTLFPPSSEELQ ANKATLVCLISDFYPGAVTV AWKADSSPVKAGVETTPSK					
70	80	90	100		
*	*	*	*		
QSNNKYAASSYLSLTPEQWK SHRSYSCQVTHEGSTVEKTV APTECS*					



12/60

Fig.15.

Amino acid sequence of the soluble IL-6R α domain

Sequence Range: 1 to 360

10	20	30	40	50	60
*	*	*	*	*	*
MVAVGCALLAALLAAPGAAL APRRCPAQEVARGVLTSLPG DSVTLTCPGVEPEDNATVHW					
70	80	90	100	110	120
*	*	*	*	*	*
VLRKPAAGSHPSRWAGMGRR LLLRSVQLHDSGNYSCYRAG RPAGTVHLLVDVPPEEPQLS					
130	140	150	160	170	180
*	*	*	*	*	*
CFRKSPLSNVVCEWGPRSTP SLTTKAVLLVRKFQNSPAED FQEPCQYSQESQKFSCQLAV					
190	200	210	220	230	240
*	*	*	*	*	*
PEGDSSFYIVSMCVASSVGS KFSKTQTFQGCGILQPDPAA NITVTAVARNPRWLSVTWQD					
250	260	270	280	290	300
*	*	*	*	*	*
PHSWNSSFYRLRFELRYRAE RSKTFTTWMVKDLQHHCVIH DAWSGLRHVQLRAQEEFGQ					
310	320	330	340	350	360
*	*	*	*	*	*
GEWSEWSPEAMGTPWTESRS PPAENEVSTPMQALTTNKDD DNILFRDSANATSLPVQDAG					

Fig.16.

Amino acid sequence of the soluble IL-6K α 313 domain

Sequence Range: 1 to 315

10	20	30	40	50	60
*	*	*	*	*	*
MVAVGCALLAALLAAPGAAL APRRCPAQEVARGVLTSLPG DSVTLTCPGVEPEDNATVHW					
70	80	90	100	110	120
*	*	*	*	*	*
VLRKPAAGSHPSRWAGMGRR LLLRSVQLHDSGNYSCYRAG RPAGTVHLLVDVPPEEPQLS					
130	140	150	160	170	180
*	*	*	*	*	*
CFRKSPLSNVVCEWGPRSTP SLTTKAVLLVRKFQNSPAED FQEPCQYSQESQKFSCQLAV					
190	200	210	220	230	240
*	*	*	*	*	*
PEGDSSFYIVSMCVASSVGS KFSKTQTFQGCGILQPDPAA NITVTAVARNPRWLSVTWQD					
250	260	270	280	290	300
*	*	*	*	*	*
PHSWNSSFYRLRFELRYRAE RSKTFTTWMVKDLQHHCVIH DAWSGLRHVQLRAQEEFGQ					
310					
*					
GEWSEWSPEAMGTTG					

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A



13/60

Fig.17.

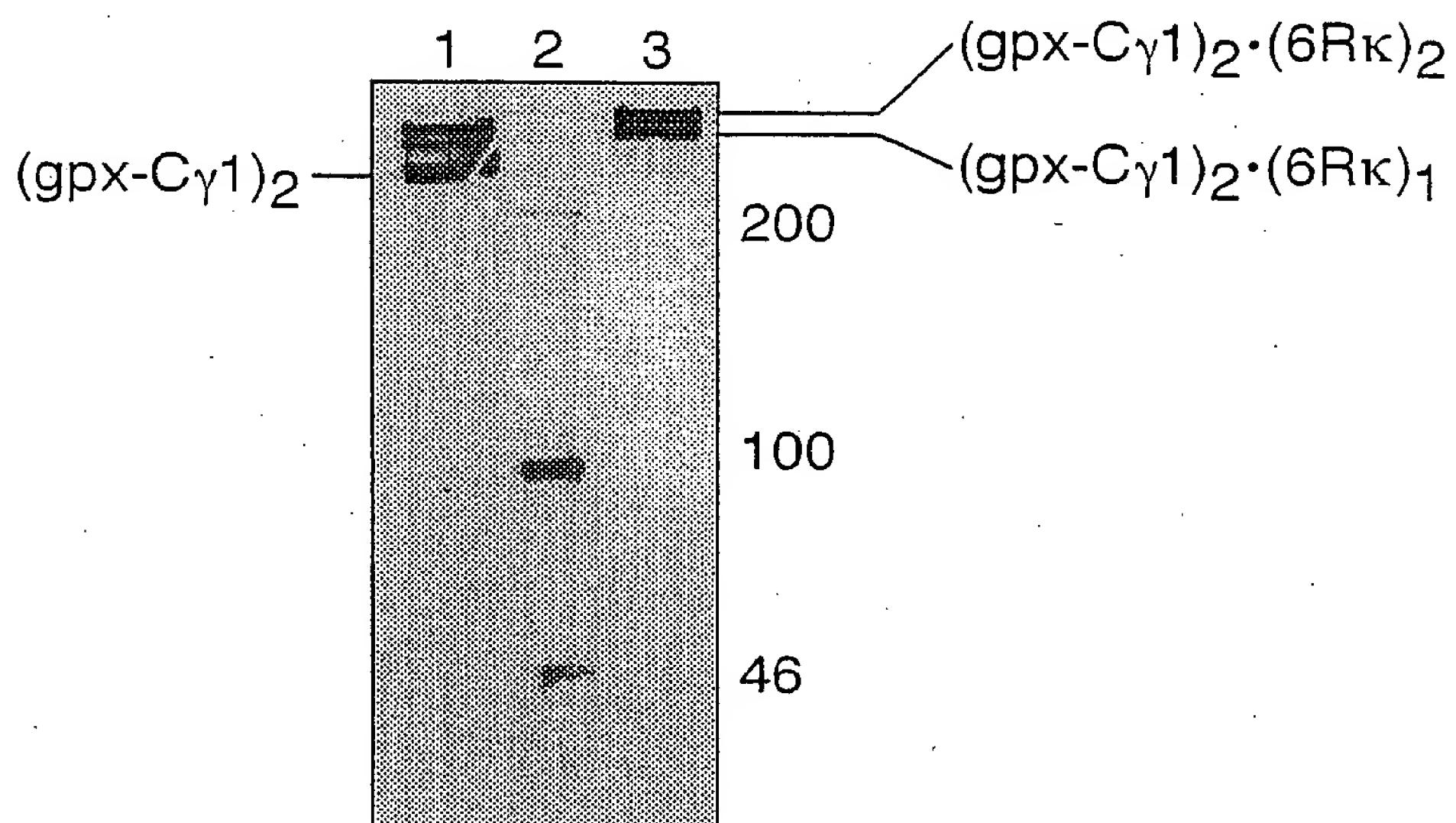
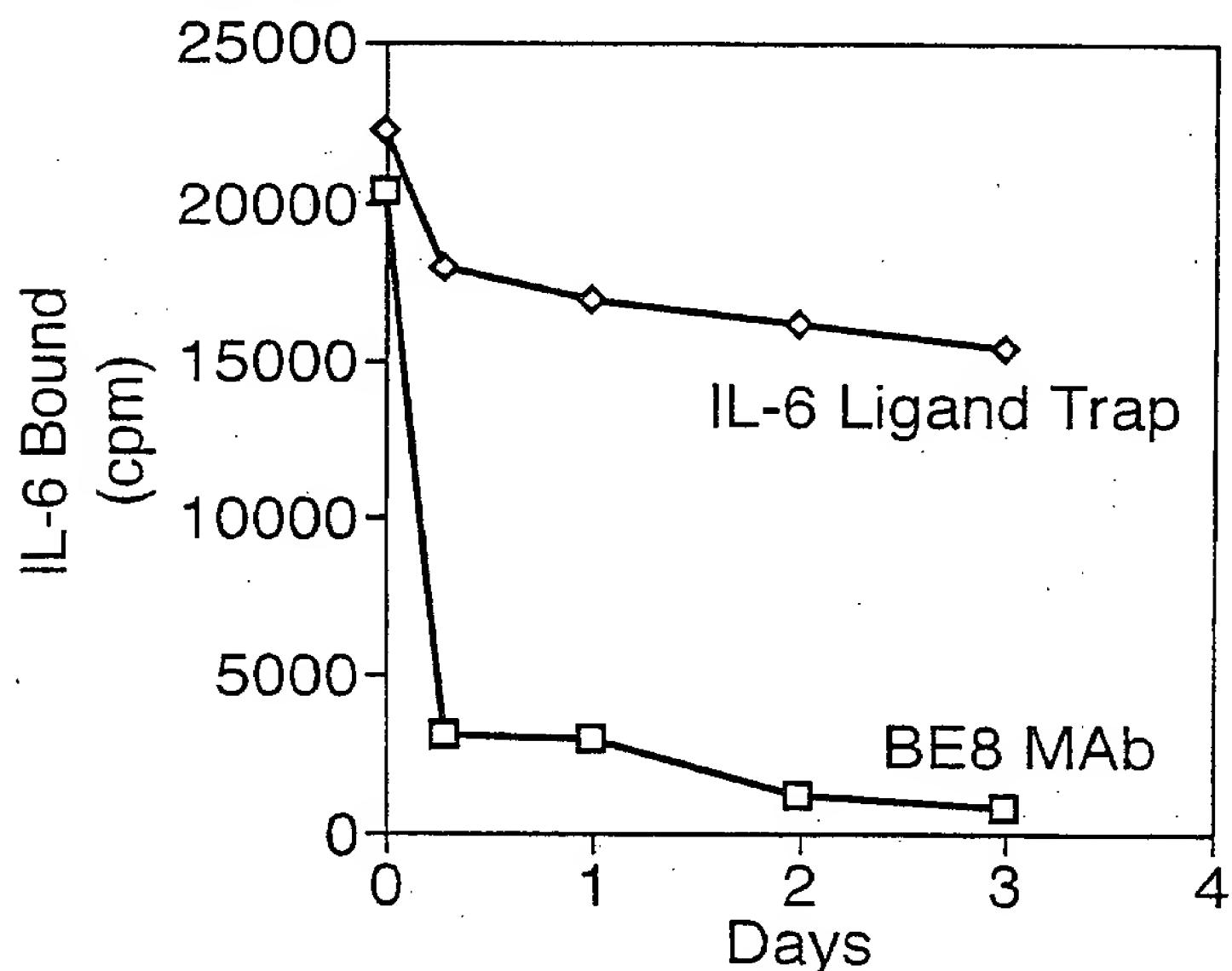
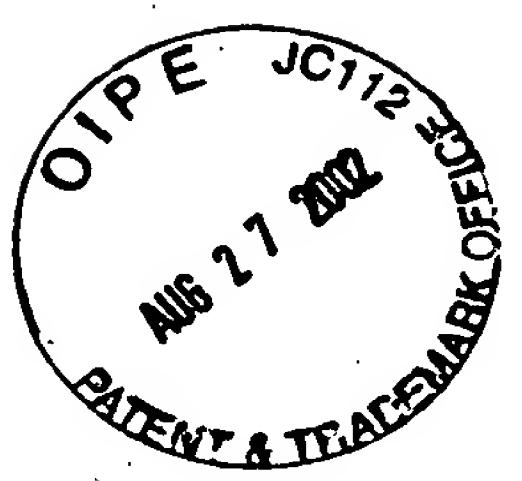


Fig.18.

IL-6 Dissociates Slowly from the Ligand Trap



Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A



14/60

Protein A binding

No Protein A binding

Does IL-6 Induce Complex Formation ?

Fig. 19A

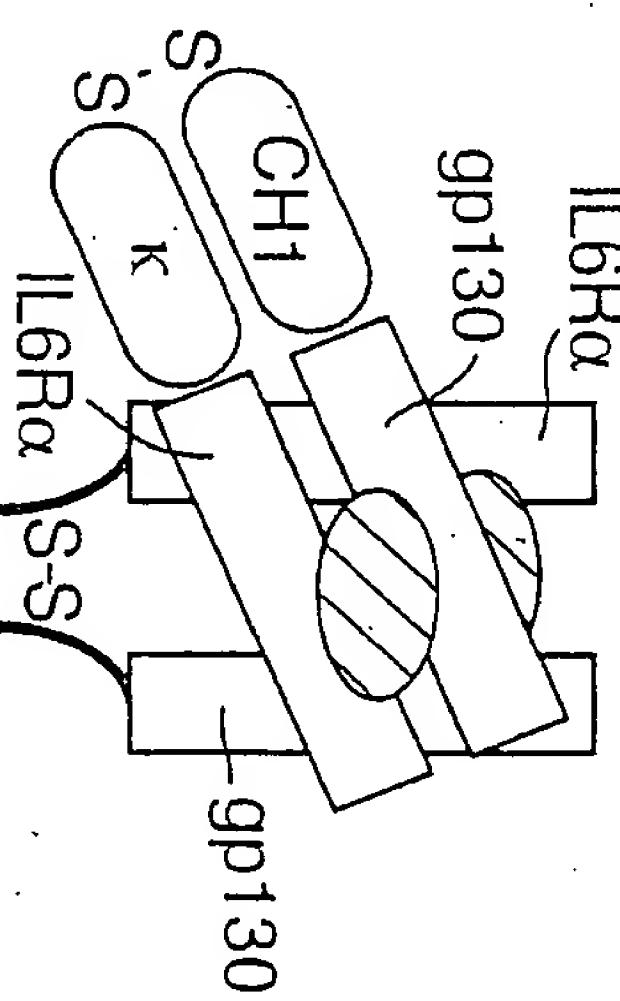
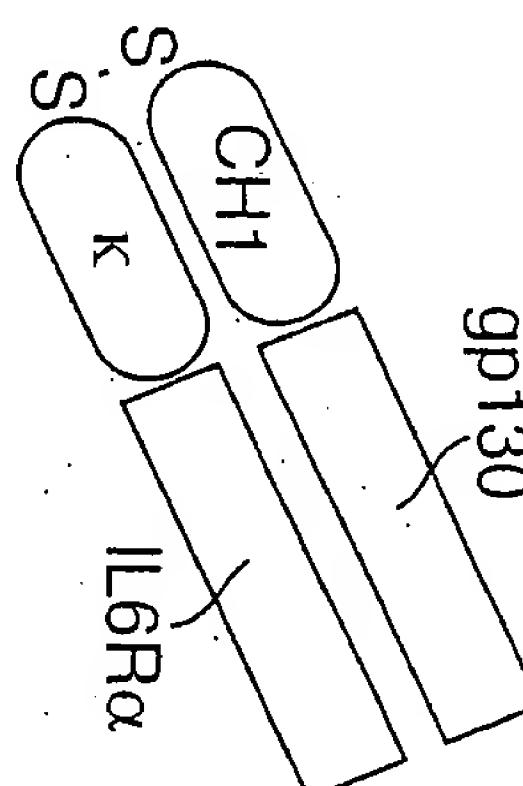
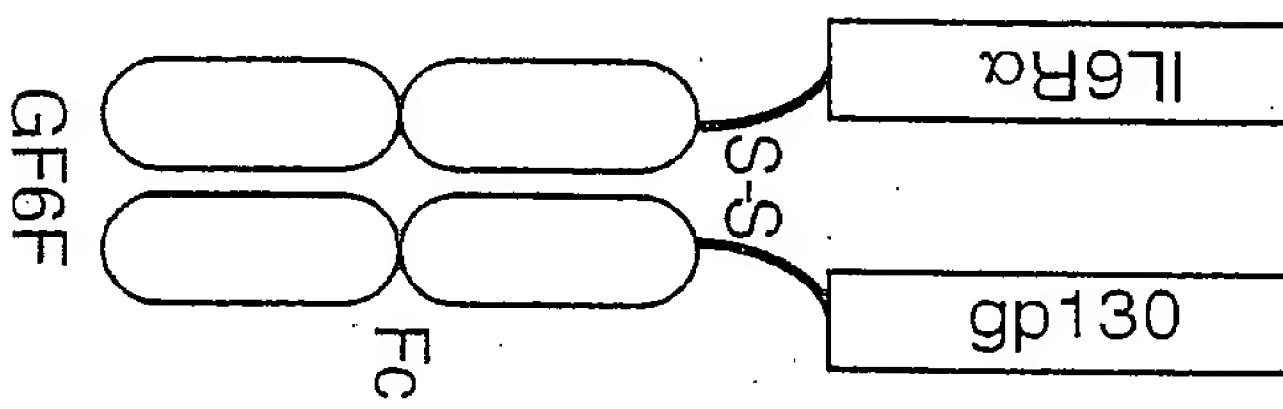
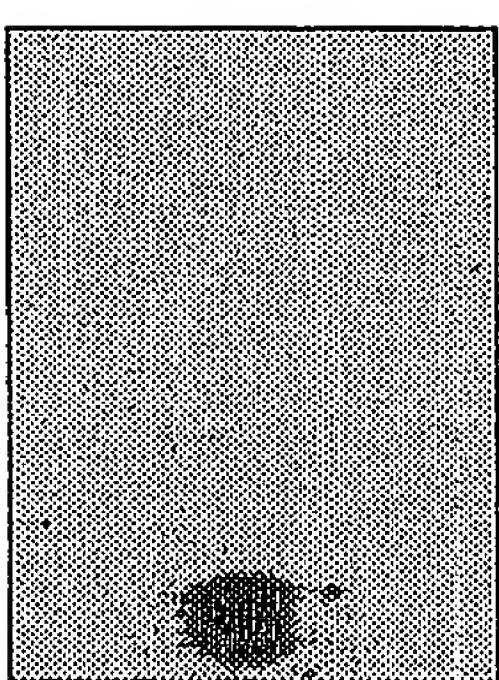


Fig. 19B

GF6F

&

GF6F G16K G16K
 - + - +
 IL-6 - + - +



IP: Prot A

Blot: α -kappa

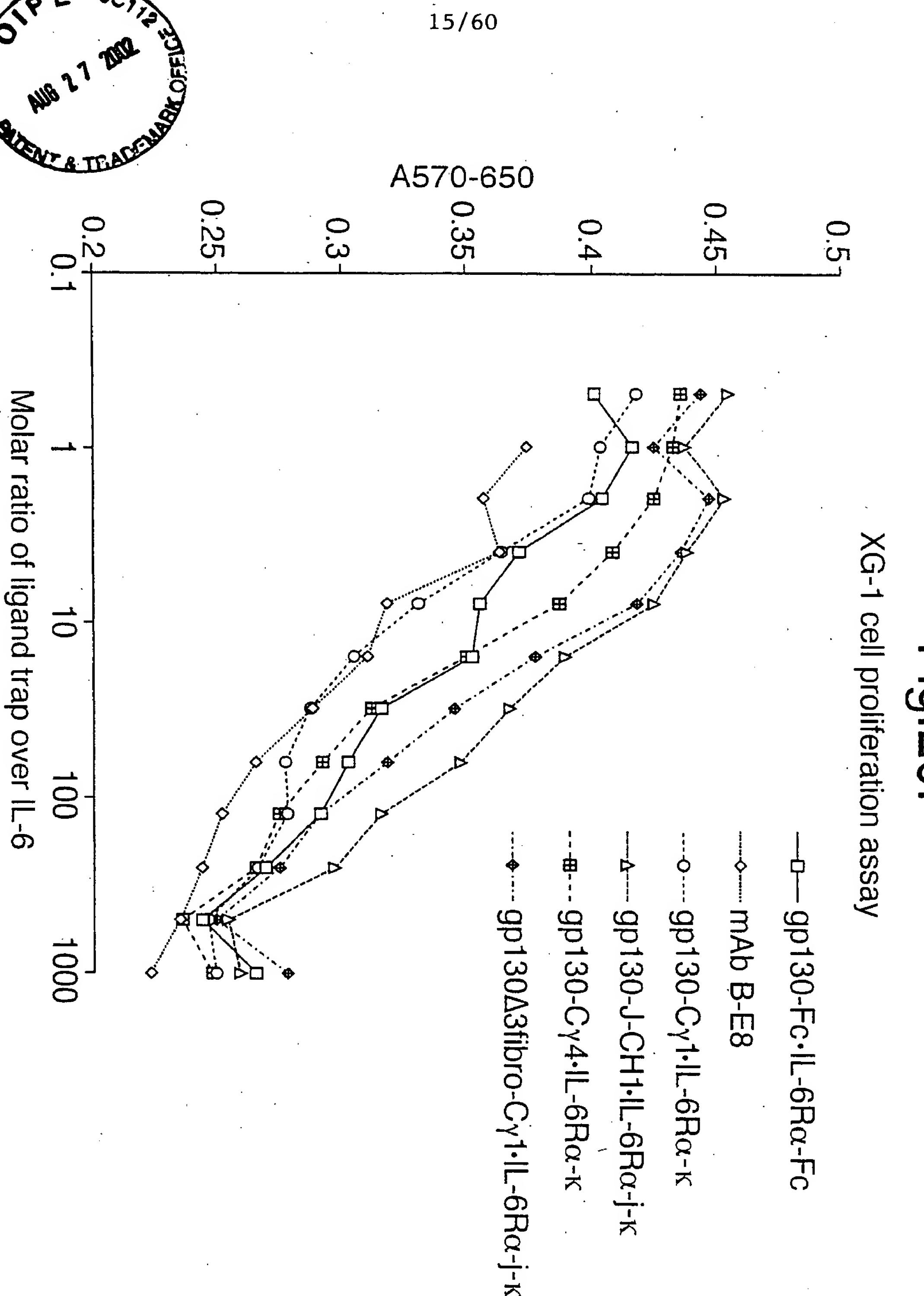


Fig.20.

XG-1 cell proliferation assay

16/60

Fig.21A.

10 20 30 40
* * * * * *
ATG GTG AAG CCA TCA TTA CCA TTC ACA TCC CTC TTA TTC CTG CAG CTG
Met Val Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu>

50 60 70 80 90
* * * * * * *
GCC CTG CTG GGA GTG GGG CTG AAC ACG ACA ATT CTG ACG CCC AAT GGG
Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly>

100 110 120 130 140
* * * * * * *
AAT GAA GAC ACC ACA GCT GAT TTC TTC CTG ACC ACT ATG CCC ACT GAC
Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp>

150 160 170 180 190
* * * * * * *
TCC CTC AGT GTT TCC ACT CTG CCC CTC CCA GAG GTT CAG TGT TTT GTG
Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val>

200 210 220 230 240
* * * * * * *
TTC AAT GTC GAG TAC ATG AAT TGC ACT TGG AAC AGC AGC TCT GAG CCC
Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Glu Pro>

250 260 270 280
* * * * * * *
CAG CCT ACC AAC CTC ACT CTG CAT TAT TGG TAC AAG AAC TCG GAT AAT
Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn>

290 300 310 320 330
* * * * * * *
GAT AAA GTC CAG AAG TGC AGC CAC TAT CTA TTC TCT GAA GAA ATC ACT
Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr>

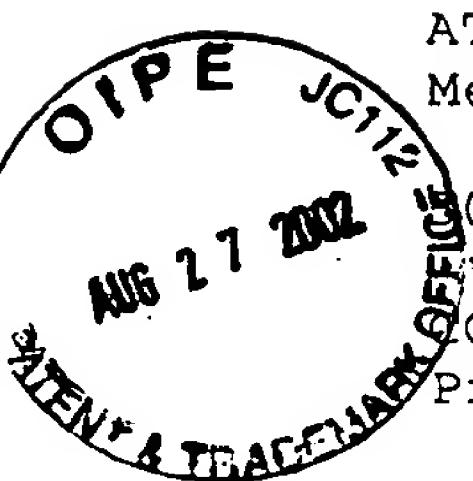
340 350 360 370 380
* * * * * * *
TCT GGC TGT CAG TTG CAA AAA AAG GAG ATC CAC CTC TAC CAA ACA TTT
Ser Gly Cys Gln Leu Gln Lys Lys Glu Ile His Leu Tyr Gln Thr Phe>

390 400 410 420 430
* * * * * * *
GTT GTT CAG CTC CAG GAC CCA CGG GAA CCC AGG AGA CAG GCC ACA CAG
Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln>

440 450 460 470 480
* * * * * * *
ATG CTA AAA CTG CAG AAT CTG GTG ATC CCC TGG GCT CCA GAG AAC CTA
Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu>

490 500 510 520
* * * * * * *
ACA CTT CAC AAA CTG AGT GAA TCC CAG CTA GAA CTG AAC TGG AAC AAC
Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn>

530 540 550 560 570
* * * * * * *
AGA TTC TTG AAC CAC TGT TTG GAG CAC TTG GTG CAG TAC CGG ACT GAC
Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp>



17/60

Fig.21B.

580 590 600 610 620
* * * * *
TGG GAC CAC AGC TGG ACT GAA CAA TCA GTG GAT TAT AGA CAT AAG TTC
Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe>

630 640 650 660 670
* * * * *
TCC TTG CCT AGT GTG GAT GGG CAG AAA CGC TAC ACG TTT CGT GTT CGG
Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg>

680 690 700 710 720
* * * * *
AGC CGC TTT AAC CCA CTC TGT GGA AGT GCT CAG CAT TGG AGT GAA TGG
Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp>

730 740 750 760
* * * * *
AGC CAC CCA ATC CAC TGG GGG AGC AAT ACT TCA AAA GAG AAC GCG TCG
Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Ala Ser>

770 780 790 800 810
* * * * *
TCT GGG AAC ATG AAG GTC CTG CAG GAG CCC ACC TGC GTC TCC GAC TAC
Ser Gly Asn Met Lys Val Leu Gln Glu Pro Thr Cys Val Ser Asp Tyr>

820 830 840 850 860
* * * * *
ATG AGC ATC TCT ACT TGC GAG TGG AAG ATG AAT GGT CCC ACC AAT TGC
Met Ser Ile Ser Thr Cys Glu Trp Lys Met Asn Gly Pro Thr Asn Cys>

870 880 890 900 910
* * * * *
AGC ACC GAG CTC CGC CTG TTG TAC CAG CTG GTT TTT CTG CTC TCC GAA
Ser Thr Glu Leu Arg Leu Tyr Gln Leu Val Phe Leu Leu Ser Glu>

920 930 940 950 960
* * * * *
GCC CAC ACG TGT ATC CCT GAG AAC AAC GGA GGC GCG GGG TGC GTG TGC
Ala His Thr Cys Ile Pro Glu Asn Asn Gly Gly Ala Gly Cys Val Cys>

970 980 990 1000
* * * * *
CAC CTG CTC ATG GAT GAC GTG GTC AGT GCG GAT AAC TAT ACA CTG GAC
His Leu Leu Met Asp Asp Val Val Ser Ala Asp Asn Tyr Thr Leu Asp>

1010 1020 1030 1040 1050
* * * * *
CTG TGG GCT GGG CAG CAG CTG CTG TGG AAG GGC TCC TTC AAG CCC AGC
Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys Gly Ser Phe Lys Pro Ser>

1060 1070 1080 1090 1100
* * * * *
GAG CAT GTG AAA CCC AGG GCC CCA GGA AAC CTG ACA GTT CAC ACC AAT
Glu His Val Lys Pro Arg Ala Pro Gly Asn Leu Thr Val His Thr Asn>

1110 1120 1130 1140 1150
* * * * *
GTC TCC GAC ACT CTG CTG ACC TGG AGC AAC CCG TAT CCC CCT GAC
Val Ser Asp Thr Leu Leu Leu Thr Trp Ser Asn Pro Tyr Pro Pro Asp>

1160 1170 1180 1190 1200
* * * * *



18/60

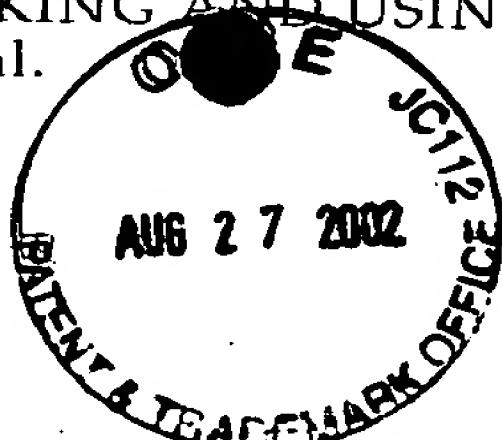


Fig. 21C.

AAT TAC CTG TAT AAT CAT CTC ACC TAT GCA GTC AAC ATT TGG AGT GAA
 Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala Val Asn Ile Trp Ser Glu>

1210 1220 1230 1240

AAC GAC CCG GCA GAT TTC AGA ATC TAT AAC GTG ACC TAC CTA GAA CCC
Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn Val Thr Tyr Leu Glu Pro

1250 1260 1270 1280 1280

1260 1270 1280 1290

1300 1310 1320 1330 1340

* * * * *
GCA CGG GTG AGG GCC TGG GCT CAG TGC TAT AAC ACC ACC TGG AGT GAG
Ala Arg Val Arg Ala Trp Ala Glu Cys Tyr Asp Thr Thr Tyr Ser Glu

1350 1360 1370 1380 1390

* * * * * * * * * * *
TGG AGC CCC AGC ACC AAG TGG CAC AAC TCC TAC AGG GAG CCC TTC GAG
Trp Ser Pro Ser Thr Lys Trp His Asp Ser Tyr Arg Glu Pro Phe Gl

1400 1410 1420 1430

* * * * * * * * * * * * *
CAG TCC GGA GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA
Gln Ser Glu Asp Lys Thr Tyr Ala Thr Glu Pro Pro Ser Ile Val

1450 1460 1470

* * * * * * * * * * *
CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Ile Phe Lys

1480 1500 1550 1580

1640 1650 1660 1670

1680 1700 1710 1730

1730 1740 1750 1760



19/60

Fig.21D.

1780	1790	1800	1810	1820											
*	*	*	*	*											
CCA	CAG	GTG	TAC	ACC	CTG	CCC	CCA	TCC	CGG	GAG	GAG	ATG	ACC	AAG	AAC
Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn>
1830	1840	1850	1860	1870											
*	*	*	*	*											
CAG	GTC	AGC	CTG	ACC	TGC	CTG	GTC	AAA	GGC	TTC	TAT	CCC	AGC	GAC	ATC
Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile>
1880	1890	1900	1910	1920											
*	*	*	*	*											
GCC	GTG	GAG	TGG	GAG	AGC	AAT	GGG	CAG	CCG	GAG	AAC	AAC	TAC	AAG	ACC
Ala	Val	Glu	Trp	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr>	
1930	1940	1950	1960												
*	*	*	*												
ACG	CCT	CCC	GTG	CTG	GAC	TCC	GAC	GGC	TCC	TTC	TTC	CTC	TAT	AGC	AAG
Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys>
1970	1980	1990	2000	2010											
*	*	*	*	*											
CTC	ACC	GTG	GAC	AAG	AGC	AGG	TGG	CAG	CAG	GGG	AAC	GTC	TTC	TCA	TGC
Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys>
2020	2030	2040	2050	2060											
*	*	*	*	*											
TCC	GTG	ATG	CAT	GAG	GCT	CTG	CAC	AAC	CAC	TAC	ACG	CAG	AAG	AGC	CTC
Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu>
2070	2080														
*	*	*	*	*											
TCC	CTG	TCT	CCG	GGT	AAA	TGA									
Ser	Leu	Ser	Pro	Gly	Lys	***>									

20/60

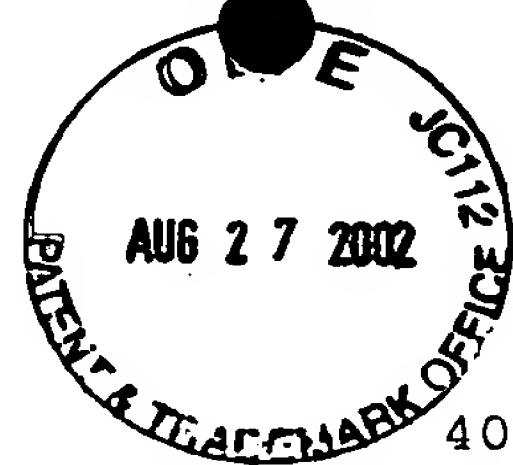


Fig.22A.

10 20 30 40
* * * * * * * * * * * *
ATG GTG AAG CCA TCA TTA CCA TTC ACA TCC CTC TTA TTC CTG CAG CTG
Met Val Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu>

50 60 70 80 90
* * * * * * * * * * * *
CCC CTG CTG GGA GTG GGG CTG AAC ACG ACA ATT CTG ACG CCC AAT GGG
Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly>

100 110 120 130 140
* * * * * * * * * * * *
AAT GAA GAC ACC ACA GCT GAT TTC TTC CTG ACC ACT ATG CCC ACT GAC
Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp>

150 160 170 180 190
* * * * * * * * * * * *
TCC CTC AGT GTT TCC ACT CTG CCC CTC CCA GAG GTT CAG TGT TTT GTG
Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val>

200 210 220 230 240
* * * * * * * * * * * *
TTC AAT GTC GAG TAC ATG AAT TGC ACT TGG AAC AGC AGC TCT GAG CCC
Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Glu Pro>

250 260 270 280
* * * * * * * * * * * *
CAG CCT ACC AAC CTC ACT CTG CAT TAT TGG TAC AAG AAC TCG GAT AAT
Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn>

290 300 310 320 330
* * * * * * * * * * * *
GAT AAA GTC CAG AAG TGC AGC CAC TAT CTA TTC TCT GAA GAA ATC ACT
Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr>

340 350 360 370 380
* * * * * * * * * * * *
TCT GGC TGT CAG TTG CAA AAA AAG GAG ATC CAC CTC TAC CAA ACA TTT
Ser Gly Cys Gln Leu Gln Lys Lys Glu Ile His Leu Tyr Gln Thr Phe>

390 400 410 420 430
* * * * * * * * * * * *
GTT GTT CAG CTC CAG GAC CCA CGG GAA CCC AGG AGA CAG GCC ACA CAG
Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln>

440 450 460 470 480
* * * * * * * * * * * *
ATG CTA AAA CTG CAG AAT CTG GTG ATC CCC TGG GCT CCA GAG AAC CTA
Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu>

490 500 510 520
* * * * * * * * * * * *
ACA CTT CAC AAA CTG AGT GAA TCC CAG CTA GAA CTG AAC TGG AAC AAC
Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn>

530 540 550 560 570
* * * * * * * * * * * *
AGA TTC TTG AAC CAC TGT TTG GAG CAC TTG GTG CAG TAC CGG ACT GAC
Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp>

21/60

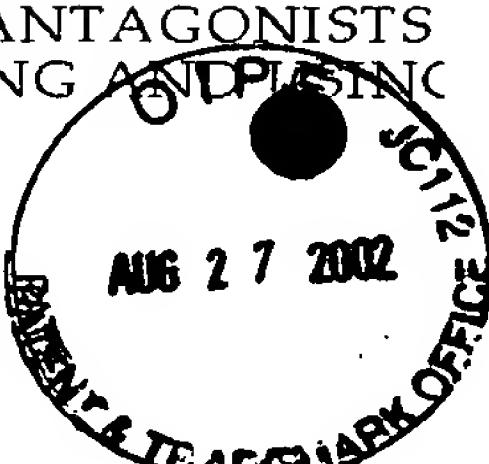


Fig.22B.

580 590 600 610 620
* * * * * * * * * * * * * * * * * * * *
TGG GAC CAC AGC TGG ACT GAA CAA TCA GTG GAT TAT AGA CAT AAG TTC
Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe>

630 640 650 660 670
* * * * * * * * * * * * * * * * * * * *
TCC TTG CCT AGT GTG GAT GGG CAG AAA CGC TAC ACG TTT CGT GTT CGG
Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg>

680 690 700 710 720
* * * * * * * * * * * * * * * * * * * *
AGC CGC TTT AAC CCA CTC TGT GGA AGT GCT CAG CAT TGG AGT GAA TGG
Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp>

730 740 750 760
* * * * * * * * * * * * * * * * * * * *
AGC CAC CCA ATC CAC TGG GGG AGC AAT ACT TCA AAA GAG AAC GGG AAC
Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Gly Asn>

770 780 790 800 810
* * * * * * * * * * * * * * * * * * * *
ATG AAG GTC CTG CAG GAG CCC ACC TGC GTC TCC GAC TAC ATG AGC ATC
Met Lys Val Leu Gln Glu Pro Thr Cys Val Ser Asp Tyr Met Ser Ile>

820 830 840 850 860
* * * * * * * * * * * * * * * * * * * *
TCT ACT TGC GAG TGG AAG ATG AAT GGT CCC ACC AAT TGC AGC ACC GAG
Ser Thr Cys Glu Trp Lys Met Asn Gly Pro Thr Asn Cys Ser Thr Glu>

870 880 890 900 910
* * * * * * * * * * * * * * * * * * * *
CTC CGC CTG TTG TAC CAG CTG GTT TTT CTG CTC TCC GAA GCC CAC ACG
Leu Arg Leu Tyr Gln Leu Val Phe Leu Leu Ser Glu Ala His Thr>

920 930 940 950 960
* * * * * * * * * * * * * * * * * * * *
TGT ATC CCT GAG AAC AAC GGA GGC GCG GGG TGC GTG TGC CAC CTG CTC
Cys Ile Pro Glu Asn Asn Gly Gly Ala Gly Cys Val Cys His Leu Leu>

970 980 990 1000
* * * * * * * * * * * * * * * * * * * *
ATG GAT GAC GTG GTC AGT GCG GAT AAC TAT ACA CTG GAC CTG TGG GCT
Met Asp Asp Val Val Ser Ala Asp Asn Tyr Thr Leu Asp Leu Trp Ala>

1010 1020 1030 1040 1050
* * * * * * * * * * * * * * * * * * * *
GGG CAG CAG CTG CTG TGG AAG GGC TCC TTC AAG CCC AGC GAG CAT GTG
Gly Gln Gln Leu Leu Trp Lys Gly Ser Phe Lys Pro Ser Glu His Val>

1060 1070 1080 1090 1100
* * * * * * * * * * * * * * * * * * * *
AAA CCC AGG GCC CCA GGA AAC CTG ACA GTT CAC ACC AAT GTC TCC GAC
Lys Pro Arg Ala Pro Gly Asn Leu Thr Val His Thr Asn Val Ser Asp>

1110 1120 1130 1140 1150
* * * * * * * * * * * * * * * * * * * *
ACT CTG CTG CTG ACC TGG AGC AAC CCG TAT CCC CCT GAC AAT TAC CTG
Thr Leu Leu Leu Thr Trp Ser Asn Pro Tyr Pro Pro Asp Asn Tyr Leu>

1160 1170 1180 1190 1200
* * * * * * * * * * * * * * * * * * * *

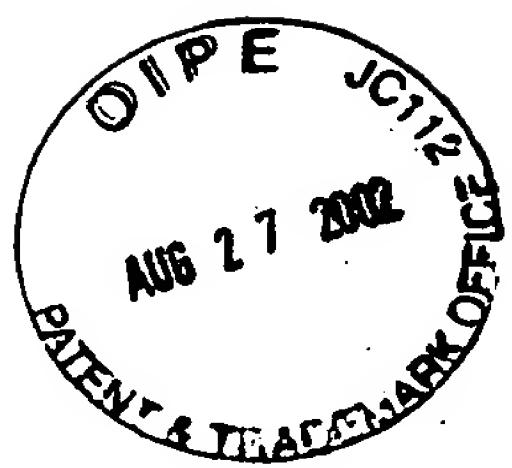


22/60

Fig.22C.

TAT AAT CAT CTC ACC TAT GCA GTG AAC ATT TGG AGT GAA AAC GAC CCG
Tyr Asn His Leu Thr Tyr Ala Val Asn Ile Trp Ser Glu Asn Asp Pro>

1210	1220	1230	1240	
*	*	*	*	*
GCA GAT TTC AGA ATC TAT AAC GTG ACC TAC CTA GAA CCC TCC CTC CGC Ala Asp Phe Arg Ile Tyr Asn Val Thr Tyr Leu Glu Pro Ser Leu Arg>				
1250	1260	1270	1280	1290
*	*	*	*	*
ATC GCA GCC AGC ACC CTG AAG TCT GGG ATT TCC TAC AGG GCA CGG GTG Ile Ala Ala Ser Thr Leu Lys Ser Gly Ile Ser Tyr Arg Ala Arg Val>				
1300	1310	1320	1330	1340
*	*	*	*	*
AGG GCC TGG GCT CAG AGC TAT AAC ACC ACC TGG AGT GAG TGG AGC CCC Arg Ala Trp Ala Gln Ser Tyr Asn Thr Thr Trp Ser Glu Trp Ser Pro>				
1350	1360	1370	1380	1390
*	*	*	*	*
AGC ACC AAG TGG CAC AAC TCC TAC AGG GAG CCC TTC GAG CAG TCC GGA Ser Thr Lys Trp His Asn Ser Tyr Arg Glu Pro Phe Glu Gln Ser Gly>				
1400	1410	1420	1430	1440
*	*	*	*	*
GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA CTC CTG GGG Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly>				
1450	1460	1470	1480	
*	*	*	*	*
GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met>				
1490	1500	1510	1520	1530
*	*	*	*	*
ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His>				
1540	1550	1560	1570	1580
*	*	*	*	*
GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val>				
1590	1600	1610	1620	1630
*	*	*	*	*
CAT AAT GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr>				
1640	1650	1660	1670	1680
*	*	*	*	*
CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly>				
1690	1700	1710	1720	
*	*	*	*	*
AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile>				
1730	1740	1750	1760	1770
*	*	*	*	*
GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA CCA CAG GTG Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val>				



23/60

Fig.22D.

1780	1790	1800	1810	1820
*	*	*	*	*
TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC CAG GTC AGC				
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser>				
1830	1840	1850	1860	1870
*	*	*	*	*
CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG				
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu>				
1880	1890	1900	1910	1920
*	*	*	*	*
TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC				
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro>				
1930	1940	1950	1960	
*	*	*	*	*
GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAT AGC AAG CTC ACC GTG				
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val>				
1970	1980	1990	2000	2010
*	*	*	*	*
GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG				
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met>				
2020	2030	2040	2050	2060
*	*	*	*	*
CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT				
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser>				
2070				
*	*	*		
CCG GGT AAA TGA				
Pro Gly Lys ***>				

24/60

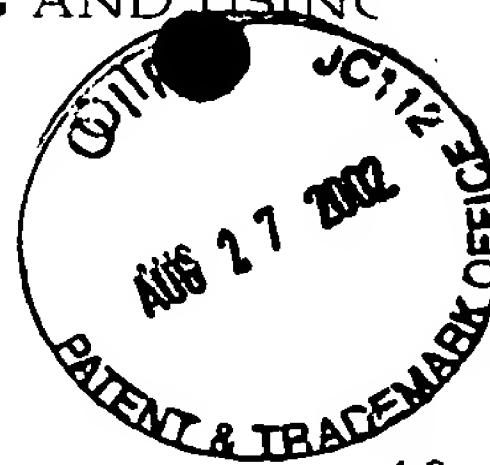


Fig.23A.

10 20 30 40
* * * * * * * *
ATG GTG AAG CCA TCA TTA CCA TTC ACA TCC CTC TTA TTC CTG CAG CTG
Met Val Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu>

50 60 70 80 90
* * * * * * * * *
CCC CTG CTG GGA GTG GGG CTG AAC ACG ACA ATT CTG ACG CCC AAT GGG
Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly>

100 110 120 130 140
* * * * * * * * *
AAT GAA GAC ACC ACA GCT GAT TTC TTC CTG ACC ACT ATG CCC ACT GAC
Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp>

150 160 170 180 190
* * * * * * * * *
TCC CTC AGT GTT TCC ACT CTG CCC CTC CCA GAG GTT CAG TGT TTT GTG
Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val>

200 210 220 230 240
* * * * * * * * *
TTC AAT GTC GAG TAC ATG AAT TGC ACT TGG AAC AGC AGC TCT GAG CCC
Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Glu Pro>

250 260 270 280
* * * * * * * * *
CAG CCT ACC AAC CTC ACT CTG CAT TAT TGG TAC AAG AAC TCG GAT AAT
Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn>

290 300 310 320 330
* * * * * * * * * *
GAT AAA GTC CAG AAG TGC AGC CAC TAT CTA TTC TCT GAA GAA ATC ACT
Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr>

340 350 360 370 380
* * * * * * * * *
TCT GGC TGT CAG TTG CAA AAA AAG GAG ATC CAC CTC TAC CAA ACA TTT
Ser Gly Cys Gln Leu Gln Lys Glu Ile His Leu Tyr Gln Thr Phe>

390 400 410 420 430
* * * * * * * * *
GTT GTT CAG CTC CAG GAC CCA CGG GAA CCC AGG AGA CAG GCC ACA CAG
Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln>

440 450 460 470 480
* * * * * * * * *
ATG CTA AAA CTG CAG AAT CTG GTG ATC CCC TGG GCT CCA GAG AAC CTA
Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu>

490 500 510 520
* * * * * * * * *
ACA CTT CAC AAA CTG AGT GAA TCC CAG CTA GAA CTG AAC TGG AAC AAC
Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn>

530 540 550 560 570
* * * * * * * * *
AGA TTC TTG AAC CAC TGT TTG GAG CAC TTG GTG CAG TAC CGG ACT GAC
Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp>



25/60

Fig.23B.

580 590 600 610 620
* * * * * * * * * * * * * * * * * * * *
TGG GAC CAC AGC TGG ACT GAA CAA TCA GTG GAT TAT AGA CAT AAG TTC
Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe>

630 640 650 660 670
* * * * * * * * * * * * * * * * * * * *
TCC TTG CCT AGT GTG GAT GGG CAG AAA CGC TAC ACG TTT CGT GTT CGG
Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg>

680 690 700 710 720
* * * * * * * * * * * * * * * * * * * *
AGC CGC TTT AAC CCA CTC TGT GGA AGT GCT CAG CAT TGG AGT GAA TGG
Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp>

730 740 750 760
* * * * * * * * * * * * * * * * * * * *
AGC CAC CCA ATC CAC TGG GGG AGC AAT ACT TCA AAA GAG AAC GCG TCG
Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Ala Ser>

770 780 790 800 810
* * * * * * * * * * * * * * * * * * * *
TCT GGG AAC ATG AAG GTC CTG CAG GAG CCC ACC TGC GTC TCC GAC TAC
Ser Gly Asn Met Lys Val Leu Gln Glu Pro Thr Cys Val Ser Asp Tyr>

820 830 840 850 860
* * * * * * * * * * * * * * * * * * * *
ATG AGC ATC TCT ACT TGC GAG TGG AAG ATG AAT GGT CCC ACC AAT TGC
Met Ser Ile Ser Thr Cys Glu Trp Lys Met Asn Gly Pro Thr Asn Cys>

870 880 890 900 910
* * * * * * * * * * * * * * * * * * * *
AGC ACC GAG CTC CGC CTG TTG TAC CAG CTG GTT TTT CTG CTC TCC GAA
Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu Val Phe Leu Leu Ser Glu>

920 930 940 950 960
* * * * * * * * * * * * * * * * * * * *
GCC CAC ACG TGT ATC CCT GAG AAC AAC GGA GGC GCG GGG TGC GTG TGC
Ala His Thr Cys Ile Pro Glu Asn Asn Gly Gly Ala Gly Cys Val Cys>

970 980 990 1000
* * * * * * * * * * * * * * * * * * * *
CAC CTG CTC ATG GAT GAC GTG GTC AGT GCG GAT AAC TAT ACA CTG GAC
His Leu Leu Met Asp Asp Val Val Ser Ala Asp Asn Tyr Thr Leu Asp>

1010 1020 1030 1040 1050
* * * * * * * * * * * * * * * * * * * *
CTG TGG GCT GGG CAG CAG CTG CTG TGG AAG GGC TCC TTC AAG CCC AGC
Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys Gly Ser Phe Lys Pro Ser>

1060 1070 1080 1090 1100
* * * * * * * * * * * * * * * * * * * *
GAG CAT GTG AAA CCC AGG GCC CCA GGA AAC CTG ACA GTT CAC ACC AAT
Glu His Val Lys Pro Arg Ala Pro Gly Asn Leu Thr Val His Thr Asn>

1110 1120 1130 1140 1150
* * * * * * * * * * * * * * * * * * * *
GTC TCC GAC ACT CTG CTG CTG ACC TGG AGC AAC CCG TAT CCC CCT GAC
Val Ser Asp Thr Leu Leu Leu Thr Trp Ser Asn Pro Tyr Pro Pro Asp>

1160 1170 1180 1190 1200
* * * * * * * * * * * * * * * * * * * *



Fig.23C.

AAT TAC CTG TAT AAT CAT CTC ACC TAT GCA GTC AAC ATT TGG AGT GAA
Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala Val Asn Ile Trp Ser Glu>

1210 1220 1230 1240
* * * * * * * *
AAC GAC CCG GCA GAT TTC AGA ATC TAT AAC GTG ACC TAC CTA GAA CCC
Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn Val Thr Tyr Leu Glu Pro>

1250 1260 1270 1280 1290
* * * * * * * * *
TCC CTC CGC ATC GCA GCC AGC ACC CTG AAG TCT GGG ATT TCC TAC AGG
Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys Ser Gly Ile Ser Tyr Arg>

1300 1310 1320 1330 1340
* * * * * * * *
GCA CGG GTG AGG GCC TGG GCT CAG AGC TAT AAC ACC ACC TGG AGT GAG
Ala Arg Val Arg Ala Trp Ala Gln Ser Tyr Asn Thr Thr Trp Ser Glu>

1350 1360 1370 1380 1390
* * * * * * * * *
TGG AGC CCC AGC ACC AAG TGG CAC AAC TCC TAC AGG GAG CCC TTC GAG
Trp Ser Pro Ser Thr Lys Trp His Asn Ser Tyr Arg Glu Pro Phe Glu>

1400 1410 1420 1430 1440
* * * * * * * * *
CAG TCC GGA GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA
Gln Ser Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu>

1450 1460 1470 1480
* * * * * * * * *
CTC CTG GGG GGA CCG TCA GTC TTC CTC CCC CCA AAA CCC AAG GAC
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp>

1490 1500 1510 1520 1530
* * * * * * * * *
ACC CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp>

1540 1550 1560 1570 1580
* * * * * * * * *
GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly>

1590 1600 1610 1620 1630
* * * * * * * * *
GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn>

1640 1650 1660 1670 1680
* * * * * * * * *
AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp>

1690 1700 1710 1720
* * * * * * * *
CTG AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro>

1730 1740 1750 1760 1770
* * * * * * * * *

GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu>

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A

27/60



Fig.23D.

1780	1790	1800	1810	1820
*	*	*	*	*
CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC				
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn>				
1830	1840	1850	1860	1870
*	*	*	*	*
CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC				
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile>				
1880	1890	1900	1910	1920
*	*	*	*	*
GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC				
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr>				
1930	1940	1950	1960	
*	*	*	*	*
ACG CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAT AGC AAG				
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys>				
1970	1980	1990	2000	2010
*	*	*	*	*
CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC				
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys>				
2020	2030	2040	2050	2060
*	*	*	*	*
TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC				
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu>				
2070	2080			
*	*	*	*	*
TCC CTG TCT CCG GGT AAA TGA				
Ser Leu Ser Pro Gly Lys ***>				



28/60

Fig.24A.

10 20 30 40
* * * * * * * *
ATG GTG GCC GTC GGC TGC GCG CTG CTG GCT GCC CTG CTG GCC GCG CCG
Met Val Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro>

50 60 70 80 90
* * * * * * * * *
GGA GCG GCG CTG GCC CCA AGG CGC TGC CCT GCG CAG GAG GTG GCA AGA
Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg>

100 110 120 130 140
* * * * * * * * *
GGC GTG CTG ACC AGT CTG CCA GGA GAC AGC GTG ACT CTG ACC TGC CCG
Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro>

150 160 170 180 190
* * * * * * * * *
GGG GTA GAG CCG GAA GAC AAT GCC ACT GTT CAC TGG GTG CTC AGG AAG
Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys>

200 210 220 230 240
* * * * * * * * *
CCG GCT GCA GGC TCC CAC CCC AGC AGA TGG GCT GGC ATG GGA AGG AGG
Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg>

250 260 270 280
* * * * * * * * *
CTG CTG CTG AGG TCG GTG CAG CTC CAC GAC TCT GGA AAC TAT TCA TGC
Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys>

290 300 310 320 330
* * * * * * * * *
TAC CGG GCC GGC CGC CCA GCT GGG ACT GTG CAC TTG CTG GTG GAT GTT
Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val>

340 350 360 370 380
* * * * * * * * *
CCC CCC GAG GAG CCC CAG CTC TCC TGC TTC CCG AAG AGC CCC CTC AGC
Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser>

390 400 410 420 430
* * * * * * * * *
AAT GTT GTT TGT GAG TGG GGT CCT CGG AGC ACC CCA TCC CTG ACG ACA
Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr>

440 450 460 470 480
* * * * * * * * *
AAG GCT GTG CTC TTG GTG AGG AAG TTT CAG AAC AGT CCG GCC GAA GAC
Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp>

490 500 510 520
* * * * * * * * *
TTC CAG GAG CCG TGC CAG TAT TCC CAG GAG TCC CAG AAG TTC TCC TGC
Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys>

530 540 550 560 570
* * * * * * * * *
CAG TTA GCA GTC CCG GAG GGA GAC AGC TCT TTC TAC ATA GTG TCC ATG
Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met>



29/60

Fig. 24B.

580 590 600 610 620
* * * * * * * * * * * * * * * * * * * *
TGC GTC GCC AGT AGT GTC GGG AGC AAG TTC AGC AAA ACT CAA ACC TTT
Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe>

630 640 650 660 670
* * * * * * * * * * * * * * * * * * * *
CAG GGT TGT GGA ATC TTG CAG CCT GAT CCG CCT GCC AAC ATC ACA GTC
Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val>

680 690 700 710 720
* * * * * * * * * * * * * * * * * * * *
ACT GCC GTG GCC AGA AAC CCC CGC TGG CTC AGT GTC ACC TGG CAA GAC
Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp>

730 740 750 760
* * * * * * * * * * * * * * * * * * * *
CCC CAC TCC TGG AAC TCA TCT TTC TAC AGA CTA CGG TTT GAG CTC AGA
Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg>

770 780 790 800 810
* * * * * * * * * * * * * * * * * * * *
TAT CGG GCT GAA CGG TCA AAG ACA TTC ACA ACA TGG ATG GTC AAG GAC
Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp>

820 830 840 850 860
* * * * * * * * * * * * * * * * * * * *
CTC CAG CAT CAC TGT GTC ATC CAC GAC GCC TGG AGC GGC CTG AGG CAC
Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His>

870 880 890 900 910
* * * * * * * * * * * * * * * * * * * *
GTG GTG CAG CTT CGT GCC CAG GAG GAG TTC GGG CAA GGC GAG TGG AGC
Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser>

920 930 940 950 960
* * * * * * * * * * * * * * * * * * * *
GAG TGG AGC CCG GAG GCC ATG GGC ACG CCT TGG ACA GAA TCC AGG AGT
Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser>

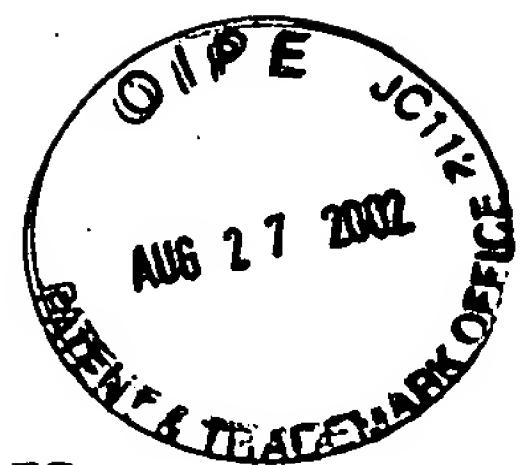
970 980 990 1000
* * * * * * * * * * * * * * * * * * * *
CCT CCA GCT GAG AAC GAG GTG TCC ACC CCC ATG ACC GGT GGC GCG CCT
Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Thr Gly Gly Ala Pro>

1010 1020 1030 1040 1050
* * * * * * * * * * * * * * * * * * * *
TCA GGT GCT CAG CTG GAA CTT CTA GAC CCA TGT GGT TAT ATC AGT CCT
Ser Gly Ala Gln Leu Glu Leu Asp Pro Cys Gly Tyr Ile Ser Pro>

1060 1070 1080 1090 1100
* * * * * * * * * * * * * * * * * * * *
GAA TCT CCA GTT GTA CAA CTT CAT TCT AAT TTC ACT GCA GTT TGT GTG
Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys Val>

1110 1120 1130 1140 1150
* * * * * * * * * * * * * * * * * * * *
CTA AAG GAA AAA TGT ATG GAT TAT TTT CAT GTA AAT GCT AAT TAC ATT
Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr Ile>

1160 1170 1180 1190 1200
* * * * * * * * * * * * * * * * * * * *



30/60

Fig.24C.

GTC TGG AAA ACA AAC CAT TTT ACT ATT CCT AAG GAG CAA TAT ACT ATC
Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr Ile>

1210 1220 1230 1240
* * * * * * *
ATA AAC AGA ACA GCA TCC AGT GTC ACC TTT ACA GAT ATA GCT TCA TTA
Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser Leu>

1250 1260 1270 1280 1290
* * * * * * * *
AAT ATT CAG CTC ACT TGC AAC ATT CTT ACA TTC GGA CAG CTT GAA CAG
Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu Gln>

1300 1310 1320 1330 1340
* * * * * * * *
AAT GTT TAT GGA ATC ACA ATA ATT TCA GGC TTG CCT CCA GAA AAA CCT
Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys Pro>

1350 1360 1370 1380 1390
* * * * * * * *
AAA AAT TTG AGT TGC ATT GTG AAC GAG GGG AAG AAA ATG AGG TGT GAG
Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys Glu>

1400 1410 1420 1430 1440
* * * * * * * *
TGG GAT GGT GGA AGG GAA ACA CAC TTG GAG ACA AAC TTC ACT TTA AAA
Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu Lys>

1450 1460 1470 1480
* * * * * * * *
TCT GAA TGG GCA ACA CAC AAG TTT GCT GAT TGC AAA GCA AAA CGT GAC
Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg Asp>

1490 1500 1510 1520 1530
* * * * * * * *
ACC CCC ACC TCA TGC ACT GTT GAT TAT TCT ACT GTG TAT TTT GTC AAC
Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val Asn>

1540 1550 1560 1570 1580
* * * * * * * *
ATT GAA GTC TGG GTA GAA GCA GAG AAT GCC CTT GGG AAG GTT ACA TCA
Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr Ser>

1590 1600 1610 1620 1630
* * * * * * * *
GAT CAT ATC AAT TTT GAT CCT GTA TAT AAA GTG AAG CCC AAT CCG CCA
Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro Pro>

1640 1650 1660 1670 1680
* * * * * * * *
CAT AAT TTA TCA GTG ATC AAC TCA GAG GAA CTG TCT AGT ATC TTA AAA
His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu Lys>

1690 1700 1710 1720
* * * * * * * *
TTG ACA TGG ACC AAC CCA AGT ATT AAG AGT GTT ATA ATA CTA AAA TAT
Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys Tyr>

1730 1740 1750 1760 1770
* * * * * * * *
AAC ATT CAA TAT AGG ACC AAA GAT GCC TCA ACT TGG AGC CAG ATT CCT
Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser Thr Trp Ser Gln Ile Pro>

31/60



Fig.24D.

1780	1790	1800	1810	1820
*	*	*	*	*
CCT GAA GAC ACA GCA TCC ACC CGA TCT TCA TTC ACT GTC CAA GAC CTT				
Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser Phe Thr Val Gln Asp Leu>				
1830	1840	1850	1860	1870
*	*	*	*	*
AAA CCT TTT ACA GAA TAT GTG TTT AGG ATT CGC TGT ATG AAG GAA GAT				
Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu Asp>				
1880	1890	1900	1910	1920
*	*	*	*	*
GGT AAG GGA TAC TGG AGT GAC TGG AGT GAA GAA GCA AGT GGG ATC ACC				
Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile Thr>				
1930	1940	1950	1960	
*	*	*	*	
TAT GAA GAT AGA CCA TCT AAA GCA CCA AGT TTC TGG TAT AAA ATA GAT				
Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser Phe Trp Tyr Lys Ile Asp>				
1970	1980	1990	2000	2010
*	*	*	*	*
CCA TCC CAT ACT CAA GGC TAC AGA ACT GTA CAA CTC GTG TGG AAG ACA				
Pro Ser His Thr Gln Gly Tyr Arg Thr Val Gln Leu Val Trp Lys Thr>				
2020	2030	2040	2050	2060
*	*	*	*	*
TTG CCT CCT TTT GAA GCC AAT GGA AAA ATC TTG GAT TAT GAA GTG ACT				
Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile Leu Asp Tyr Glu Val Thr>				
2070	2080	2090	2100	2110
*	*	*	*	*
CTC ACA AGA TGG AAA TCA CAT TTA CAA AAT TAC ACA GTT AAT GCC ACA				
Leu Thr Arg Trp Lys Ser His Leu Gln Asn Tyr Thr Val Asn Ala Thr>				
2120	2130	2140	2150	2160
*	*	*	*	*
AAA CTG ACA GTA AAT CTC ACA AAT GAT CGC TAT CTA GCA ACC CTA ACA				
Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Leu Ala Thr Leu Thr>				
2170	2180	2190	2200	
*	*	*	*	
GTA AGA AAT CTT GTT GGC AAA TCA GAT GCA GCT GTT TTA ACT ATC CCT				
Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile Pro>				
2210	2220	2230	2240	2250
*	*	*	*	*
GCC TGT GAC TTT CAA GCT ACT CAC CCT GTA ATG GAT CTT AAA GCA TTC				
Ala Cys Asp Phe Gln Ala Thr His Pro Val Met Asp Leu Lys Ala Phe>				
2260	2270	2280	2290	2300
*	*	*	*	*
CCC AAA GAT AAC ATG CTT TGG GTG GAA TGG ACT ACT CCA AGG GAA TCT				
Pro Lys Asp Asn Met Leu Trp Val Glu Trp Thr Thr Pro Arg Glu Ser>				
2310	2320	2330	2340	2350
*	*	*	*	*
GTA AAG AAA TAT ATA CTT GAG TGG TGT GTG TTA TCA GAT AAA GCA CCC				
Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala Pro>				
2360	2370	2380	2390	2400

32 / 60

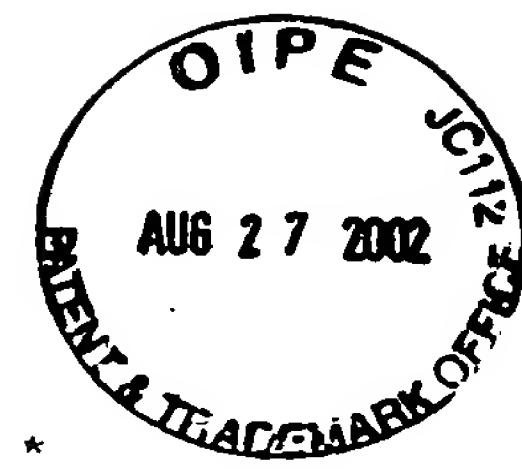


Fig. 24E.

TGT ATC ACA GAC TGG CAA CAA GAA GAT GGT ACC GTG CAT CGC ACC TAT
 Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly Thr Val His Arg Thr Tyr>

2410	2420	2430	2440
*	*	*	*
TTA AGA GGG AAC TTA GCA GAG AGC AAA TGC TAT TTG ATA ACA GTT ACT			
Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val Thr>			

2450	2460	2470	2480	2490											
*	*	*	*	*											
CCA	GTA	TAT	GCT	GAT	GGA	CCA	GGA	AGC	CCT	GAA	TCC	ATA	AAG	GCA	TAC
Pro	Val	Tyr	Ala	Asp	Gly	Pro	Gly	Ser	Pro	Glu	Ser	Ile	Lys	Ala	Tyr>

2500		2510		2520		2530		2540							
*	*	*	*	*	*	*	*	*	*						
CTT	AAA	CAA	GCT	CCA	CCT	TCC	AAA	GGA	CCT	ACT	GTT	CGG	ACA	AAA	AAA
Leu	Lys	Gln	Ala	Pro	Pro	Ser	Lys	Gly	Pro	Thr	Val	Arg	Thr	Lys	>

2550	2560	2570	2580	2590											
*	*	*	*	*											
GTA	GGG	AAA	AAC	GAA	GCT	GTC	TTA	GAG	TGG	GAC	CAA	CTT	CCT	GTT	GAT
Val	Gly	Lys	Asn	Glu	Ala	Val	Leu	Glu	Trp	Asp	Gln	Leu	Pro	Val	Asp>

2600	2610	2620	2630	2640											
*	*	*	*	*											
GTT	CAG	AAT	GGA	TTT	ATC	AGA	AAT	TAT	ACT	ATA	TTT	TAT	AGA	ACC	ATC
Val	Gln	Asn	Gly	Phe	Ile	Arg	Asn	Tyr	Thr	Ile	Phe	Tyr	Arg	Thr	Ile>

2650	2660	2670	2680												
*	*	*	*												
ATT	GGA	AAT	GAA	ACT	GCT	GTG	AAT	GTG	GAT	TCT	TCC	CAC	ACA	GAA	TAT
Ile	Gly	Asn	Glu	Thr	Ala	Val	Asn	Val	Asp	Ser	Ser	His	Thr	Glu	Tyr>

2690	2700		2710		2720		2730								
*	*	*	*	*	*	*	*	*							
ACA	TTG	TCC	TCT	TTG	ACT	AGT	GAC	ACA	TTG	TAC	ATG	GTA	CGA	ATG	GCA
Thr	Leu	Ser	Ser	Leu	Thr	Ser	Asp	Thr	Leu	Tyr	Met	Val	Arg	Met	Ala>

2740		2750		2760		2770		2780							
*	*	*	*	*	*	*	*	*							
GCA	TAC	ACA	GAT	GAA	GGT	GGG	AAG	GAT	GGT	CCA	GAA	TTC	ACT	TTT	ACT
Ala	Tyr	Thr	Asp	Glu	Gly	Gly	Lys	Asp	Gly	Pro	Glu	Phe	Thr	Phe	Thr>

2790		2800		2810		2820		2830							
*	*	*	*	*	*	*	*	*	*						
ACC	CCA	AAG	TTT	GCT	CAA	GGA	GAA	ATT	GAA	TCC	GGG	GGC	GAC	AAA	ACT
Thr	Pro	Lys	Phe	Ala	Gln	Gly	Glu	Ile	Glu	Ser	Gly	Gly	Asp	Lys	Thr>

2840	2850	2860	2870	2880											
*	*	*	*	*											
CAC	ACA	TGC	CCA	CCG	TGC	CCA	GCA	CCT	GAA	CTC	CTG	GGG	GGA	CCG	TCA
His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser>

2890	2900	2910	2920												
*	*	*	*												
GTC	TTC	CTC	TTC	CCC	CCA	AAA	CCC	AAG	GAC	ACC	CTC	ATG	ATC	TCC	CGG
Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg>

2930 2940 2950 2960 2970
* * * * * *
ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC CCT



33/60

Fig.24F.

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro>

2980 2990 3000 3010 3020
*
GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT GCC
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala>

3030 3040 3050 3060 3070
*
AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val>

3080 3090 3100 3110 3120
*
AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Glu Lys Tyr>

3130 3140 3150 3160
*
AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr>

3170 3180 3190 3200 3210
*
ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu>

3220 3230 3240 3250 3260
*
CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC CAG GTC AGC CTG ACC TGC
Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys>

3270 3280 3290 3300 3310
*
CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser>

3320 3330 3340 3350 3360
*
AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG GAC
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp>

3370 3380 3390 3400
*
TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser>

3410 3420 3430 3440 3450
*
AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala>

3460 3470 3480 3490 3500
*
CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys>

*
TGA
***>

34/60



Fig. 25A.

10 20 30 40
* * * * * * * * * * * * * * * * * * * *
ATG GTG GCC GTC GGC TGC GCG CTG CTG GCT GCC CTG CTG GCC GCG CCG
Met Val Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro>

50 60 70 80 90
* * * * * * * * * * * * * * * * * * * *
GGA GCG GCG CTG GCC CCA AGG CGC TGC CCT GCG CAG GAG GTG GCA AGA
Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg>

100 110 120 130 140
* * * * * * * * * * * * * * * * * * * *
GGC GTG CTG ACC AGT CTG CCA GGA GAC AGC GTG ACT CTG ACC TGC CCG
Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro>

150 160 170 180 190
* * * * * * * * * * * * * * * * * * * *
GGG GTA GAG CCG GAA GAC AAT GCC ACT GTT CAC TGG GTG CTC AGG AAG
Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys>

200 210 220 230 240
* * * * * * * * * * * * * * * * * * * *
CCG GCT GCA GGC TCC CAC CCC AGC AGA TGG GCT GGC ATG GGA AGG AGG
Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg>

250 260 270 280
* * * * * * * * * * * * * * * * * * * *
CTG CTG CTG AGG TCG GTG CAG CTC CAC GAC TCT GGA AAC TAT TCA TGC
Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys>

290 300 310 320 330
* * * * * * * * * * * * * * * * * * * *
TAC CGG GCC GGC CGC CCA GCT GGG ACT GTG CAC TTG CTG GTG GAT GTT
Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val>

340 350 360 370 380
* * * * * * * * * * * * * * * * * * * *
CCC CCC GAG GAG CCC CAG CTC TCC TGC TTC CGG AAG AGC CCC CTC AGC
Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser>

390 400 410 420 430
* * * * * * * * * * * * * * * * * * * *
AAT GTT GTT TGT GAG TGG GGT CCT CGG AGC ACC CCA TCC CTG ACG ACA
Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr>

440 450 460 470 480
* * * * * * * * * * * * * * * * * * * *
AAG GCT GTG CTC TTG GTG AGG AAG TTT CAG AAC AGT CCG GCC GAA GAC
Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp>

490 500 510 520
* * * * * * * * * * * * * * * * * * * *
TTC CAG GAG CCG TGC CAG TAT TCC CAG GAG TCC CAG AAG TTC TCC TGC
Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys>

530 540 550 560 570
* * * * * * * * * * * * * * * * * * * *
CAG TTA GCA GTC CCG GAG GGA GAC AGC TCT TTC TAC ATA GTG TCC ATG
Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met>



35/60

Fig.25B.

580 590 600 610 620
* * * * * * * * * * * * * * * * * * * * * * * * *
TGC GTC GCC AGT AGT GTC GGG AGC AAG TTC AGC AAA ACT CAA ACC TTT
Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe>

630 640 650 660 670
* * * * * * * * * * * * * * * * * * * * * * * * *
CAG GGT TGT GGA ATC TTG CAG CCT GAT CCG CCT GCC AAC ATC ACA GTC
Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val>

680 690 700 710 720
* * * * * * * * * * * * * * * * * * * * * * * * *
ACT GCC GTG GCC AGA AAC CCC CGC TGG CTC AGT GTC ACC TGG CAA GAC
Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp>

730 740 750 760
* * * * * * * * * * * * * * * * * * * *
CCC CAC TCC TGG AAC TCA TCT TTC TAC AGA CTA CGG TTT GAG CTC AGA
Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg>

770 780 790 800 810
* * * * * * * * * * * * * * * * * * * * * * * * *
TAT CGG GCT GAA CGG TCA AAG ACA TTC ACA ACA TGG ATG GTC AAG GAC
Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Trp Met Val Lys Asp>

820 830 840 850 860
* * * * * * * * * * * * * * * * * * * * * * * * *
CTC CAG CAT CAC TGT GTC ATC CAC GAC GCC TGG AGC GGC CTG AGG CAC
Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His>

870 880 890 900 910
* * * * * * * * * * * * * * * * * * * * * * * * *
GTG GTG CAG CTT CGT GCC CAG GAG GAG TTC GGG CAA GGC GAG TGG AGC
Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser>

920 930 940 950 960
* * * * * * * * * * * * * * * * * * * * * * * * *
GAG TGG AGC CCG GAG GCC ATG GGC ACG CCT TGG ACA GAA TCG CGA TCG
Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser>

970 980 990 1000
* * * * * * * * * * * * * * * * * * * *
CCT CCA GCT GAG AAC GAG GTG TCC ACC CCC ATG GAA CTT CTA GAC CCA
Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Glu Leu Leu Asp Pro>

1010 1020 1030 1040 1050
* * * * * * * * * * * * * * * * * * * * * * * * *
TGT GGT TAT ATC AGT CCT GAA TCT CCA GTT GTA CAA CTT CAT TCT AAT
Cys Gly Tyr Ile Ser Pro Glu Ser Pro Val Val Gln Leu His Ser Asn>

1060 1070 1080 1090 1100
* * * * * * * * * * * * * * * * * * * * * * * * *
TTC ACT GCA GTT TGT GTG CTA AAG GAA AAA TGT ATG GAT TAT TTT CAT
Phe Thr Ala Val Cys Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His>

1110 1120 1130 1140 1150
* * * * * * * * * * * * * * * * * * * * * * * * *
GTA AAT GCT AAT TAC ATT GTC TGG AAA ACA AAC CAT TTT ACT ATT CCT
Val Asn Ala Asn Tyr Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro>

1160 1170 1180 1190 1200
* * * * * * * * * * * * * * * * * * * * * * * * *



36/60

Fig.25C.

AAG GAG CAA TAT ACT ATC ATA AAC AGA ACA GCA TCC AGT GTC ACC TTT
Lys Glu Gln Tyr Thr Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe>

1210	1220	1230	1240	
*	*	*	*	*
ACA GAT ATA GCT TCA TTA AAT ATT CAG CTC ACT TGC AAC ATT CTT ACA				
Thr Asp Ile Ala Ser Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr>				
1250	1260	1270	1280	1290
*	*	*	*	*
TTC GGA CAG CTT GAA CAG AAT GTT TAT GGA ATC ACA ATA ATT TCA GGC				
Phe Gly Gln Leu Glu Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly>				
1300	1310	1320	1330	1340
*	*	*	*	*
TTG CCT CCA GAA AAA CCT AAA AAT TTG AGT TGC ATT GTG AAC GAG GGG				
Leu Pro Pro Glu Lys Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly>				
1350	1360	1370	1380	1390
*	*	*	*	*
AAG AAA ATG AGG TGT GAG TGG GAT GGT GGA AGG GAA ACA CAC TTG GAG				
Lys Lys Met Arg Cys Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu>				
1400	1410	1420	1430	1440
*	*	*	*	*
ACA AAC TTC ACT TTA AAA TCT GAA TGG GCA ACA CAC AAG TTT GCT GAT				
Thr Asn Phe Thr Leu Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp>				
1450	1460	1470	1480	
*	*	*	*	*
TGC AAA GCA AAA CGT GAC ACC CCC ACC TCA TGC ACT GTT GAT TAT TCT				
Cys Lys Ala Lys Arg Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser>				
1490	1500	1510	1520	1530
*	*	*	*	*
ACT GTG TAT TTT GTC AAC ATT GAA GTC TGG GTA GAA GCA GAG AAT GCC				
Thr Val Tyr Phe Val Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala>				
1540	1550	1560	1570	1580
*	*	*	*	*
CTT GGG AAG GTT ACA TCA GAT CAT ATC AAT TTT GAT CCT GTA TAT AAA				
Leu Gly Lys Val Thr Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys>				
1590	1600	1610	1620	1630
*	*	*	*	*
GTG AAG CCC AAT CCG CCA CAT AAT TTA TCA GTG ATC AAC TCA GAG GAA				
Val Lys Pro Asn Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu>				
1640	1650	1660	1670	1680
*	*	*	*	*
CTG TCT AGT ATC TTA AAA TTG ACA TGG ACC AAC CCA AGT ATT AAG AGT				
Leu Ser Ser Ile Leu Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser>				
1690	1700	1710	1720	
*	*	*	*	*
GTT ATA ATA CTA AAA TAT AAC ATT CAA TAT AGG ACC AAA GAT GCC TCA				
Val Ile Ile Leu Tyr Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser>				
1730	1740	1750	1760	1770
*	*	*	*	*
ACT TGG AGC CAG ATT CCT CCT GAA GAC ACA GCA TCC ACC CGA TCT TCA				
Thr Trp Ser Gln Ile Pro Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser>				

AUG 27 2002



37/60

Fig.25D.

1780	1790	1800	1810	1820
* * *	* * *	* * *	* * *	* * *
TTC ACT GTC CAA GAC CTT AAA CCT TTT ACA GAA TAT GTG TTT AGG ATT				
Phe Thr Val Gln Asp Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile>				
1830	1840	1850	1860	1870
* * *	* * *	* * *	* * *	* * *
CGC TGT ATG AAG GAA GAT GGT AAG GGA TAC TGG AGT GAC TGG AGT GAA				
Arg Cys Met Lys Glu Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu>				
1880	1890	1900	1910	1920
* * *	* * *	* * *	* * *	* * *
GAA GCA AGT GGG ATC ACC TAT GAA GAT AGA CCA TCT AAA GCA CCA AGT				
Glu Ala Ser Gly Ile Thr Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser>				
1930	1940	1950	1960	
* * *	* * *	* * *	* * *	
TTC TGG TAT AAA ATA GAT CCA TCC CAT ACT CAA GGC TAC AGA ACT GTA				
Phe Trp Tyr Lys Ile Asp Pro Ser His Thr Gln Gly Tyr Arg Thr Val>				
1970	1980	1990	2000	2010
* * *	* * *	* * *	* * *	* * *
CAA CTC GTG TGG AAG ACA TTG CCT CCT TTT GAA GCC AAT GGA AAA ATC				
Gln Leu Val Trp Lys Thr Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile>				
2020	2030	2040	2050	2060
* * *	* * *	* * *	* * *	* * *
TTG GAT TAT GAA GTG ACT CTC ACA AGA TGG AAA TCA CAT TTA CAA AAT				
Leu Asp Tyr Glu Val Thr Leu Thr Arg Trp Lys Ser His Leu Gln Asn>				
2070	2080	2090	2100	2110
* * *	* * *	* * *	* * *	* * *
TAC ACA GTT AAT GCC ACA AAA CTG ACA GTA AAT CTC ACA AAT GAT CGC				
Tyr Thr Val Asn Ala Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg>				
2120	2130	2140	2150	2160
* * *	* * *	* * *	* * *	* * *
TAT CTA GCA ACC CTA ACA GTA AGA AAT CTT GTT GGC AAA TCA GAT GCA				
Tyr Leu Ala Thr Leu Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala>				
2170	2180	2190	2200	
* * *	* * *	* * *	* * *	
GCT GTT TTA ACT ATC CCT GCC TGT GAC TTT CAA GCT ACT CAC CCT GTA				
Ala Val Leu Thr Ile Pro Ala Cys Asp Phe Gln Ala Thr His Pro Val>				
2210	2220	2230	2240	2250
* * *	* * *	* * *	* * *	* * *
ATG GAT CTT AAA GCA TTC CCC AAA GAT AAC ATG CTT TGG GTG GAA TGG				
Met Asp Leu Lys Ala Phe Pro Lys Asp Asn Met Leu Trp Val Glu Trp>				
2260	2270	2280	2290	2300
* * *	* * *	* * *	* * *	* * *
ACT ACT CCA AGG GAA TCT GTA AAG AAA TAT ATA CTT GAG TGG TGT GTG				
Thr Thr Pro Arg Glu Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val>				
2310	2320	2330	2340	2350
* * *	* * *	* * *	* * *	* * *
TTA TCA GAT AAA GCA CCC TGT ATC ACA GAC TGG CAA CAA GAA GAT GGT				
Leu Ser Asp Lys Ala Pro Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly>				
2360	2370	2380	2390	2400



38/60

Fig.25E.

ACC GTG CAT CGC ACC TAT TTA AGA GGG AAC TTA GCA GAG AGC AAA TGC
 Thr Val His Arg Thr Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys>

2410	2420	2430	2440
------	------	------	------

TAT TTG ATA ACA GTT ACT CCA GTA TAT GCT GAT GGA CCA GGA AGC CCT
 Tyr Leu Ile Thr Val Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro>

2450	2460	2470	2480	2490
------	------	------	------	------

GAA TCC ATA AAG GCA TAC CTT AAA CAA GCT CCA CCT TCC AAA GGA CCT
 Glu Ser Ile Lys Ala Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro>

2500	2510	2520	2530	2540
------	------	------	------	------

ACT GTT CGG ACA AAA AAA GTA GGG AAA AAC GAA GCT GTC TTA GAG TGG
 Thr Val Arg Thr Lys Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp>

2550	2560	2570	2580	2590
------	------	------	------	------

GAC CAA CTT CCT GTT GAT GTT CAG AAT GGA TTT ATC AGA AAT TAT ACT
 Asp Gln Leu Pro Val Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr>

2600	2610	2620	2630	2640
------	------	------	------	------

ATA TTT TAT AGA ACC ATC ATT GGA AAT GAA ACT GCT GTG AAT GTG GAT
 Ile Phe Tyr Arg Thr Ile Gly Asn Glu Thr Ala Val Asn Val Asp>

2650	2660	2670	2680
------	------	------	------

TCT TCC CAC ACA GAA TAT ACA TTG TCC TCT TTG ACT AGT GAC ACA TTG
 Ser Ser His Thr Glu Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu>

2690	2700	2710	2720	2730
------	------	------	------	------

TAC ATG GTA CGA ATG GCA GCA TAC ACA GAT GAA GGT GGG AAG GAT GGT
 Tyr Met Val Arg Met Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly>

2740	2750	2760	2770	2780
------	------	------	------	------

CCA GAA TTC ACT TTT ACT ACC CCA AAG TTT GCT CAA GGA GAA ATT GAA
 Pro Glu Phe Thr Phe Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu>

2790	2800	2810	2820	2830
------	------	------	------	------

TCC GGG GGC GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA
 Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu>

2840	2850	2860	2870	2880
------	------	------	------	------

CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC
 Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp>

2890	2900	2910	2920
------	------	------	------

ACC CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC
 Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp>

2930	2940	2950	2960	2970
------	------	------	------	------

GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC



39/60

Fig.25F.

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly>

2980 2990 3000 3010 3020
* * * * * * * * *
GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn>

3030 3040 3050 3060 3070
* * * * * * * * *
AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp>

3080 3090 3100 3110 3120
* * * * * * * * *
CTG AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro>

3130 3140 3150 3160
* * * * * * * * *
GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu>

3170 3180 3190 3200 3210
* * * * * * * * *
CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn>

3220 3230 3240 3250 3260
* * * * * * * * *
CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile>

3270 3280 3290 3300 3310
* * * * * * * * *
GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr>

3320 3330 3340 3350 3360
* * * * * * * * *
ACG CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys>

3370 3380 3390 3400
* * * * * * * * *
CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys>

3410 3420 3430 3440 3450
* * * * * * * * *
TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu>

3460 3470
* * * *
TCC CTG TCT CCG GGT AAA TGA
Ser Leu Ser Pro Gly Lys ***>



40/60

Fig.26A.

10 20 30 40
* * * * * * * *
ATG GTG CTT CTG TGG TGT GTA GTG AGT CTC TAC TTT TAT GGA ATC CTG
Met Val Leu Leu Trp Cys Val Val Ser Leu Tyr Phe Tyr Gly Ile Leu>

50 60 70 80 90
* * * * * * * * *
CAA AGT GAT GCC TCA GAA CGC TGC GAT GAC TGG GGA CTA GAC ACC ATG
Gln Ser Asp Ala Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met>

100 110 120 130 140
* * * * * * * * *
AGG CAA ATC CAA GTG TTT GAA GAT GAG CCA GCT CGC ATC AAG TGC CCA
Arg Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro>

150 160 170 180 190
* * * * * * * * *
CTC TTT GAA CAC TTC TTG AAA TTC AAC TAC AGC ACA GCC CAT TCA GCT
Leu Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala>

200 210 220 230 240
* * * * * * * * *
GGC CTT ACT CTG ATC TGG TAT TGG ACT AGG CAG GAC CGG GAC CTT GAG
Gly Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu>

250 260 270 280
* * * * * * * * *
GAG CCA ATT AAC TTC CGC CTC CCC GAG AAC CGC ATT AGT AAG GAG AAA
Glu Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys>

290 300 310 320 330
* * * * * * * * *
GAT GTG CTG TGG TTC CGG CCC ACT CTC CTC AAT GAC ACT GGC AAC TAT
Asp Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr>

340 350 360 370 380
* * * * * * * * *
ACC TGC ATG TTA AGG AAC ACT ACA TAT TGC AGC AAA GTT GCA TTT CCC
Thr Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro>

390 400 410 420 430
* * * * * * * * *
TTG GAA GTT GTT CAA AAA GAC AGC TGT TTC AAT TCC CCC ATG AAA CTC
Leu Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu>

440 450 460 470 480
* * * * * * * * *
CCA GTG CAT AAA CTG TAT ATA GAA TAT GGC ATT CAG AGG ATC ACT TGT
Pro Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys>

490 500 510 520
* * * * * * * * *
CCA AAT GTA GAT GGA TAT TTT CCT TCC AGT GTC AAA CCG ACT ATC ACT
Pro Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr>

530 540 550 560 570
* * * * * * * * *
TGG TAT ATG GGC TGT TAT AAA ATA CAG AAT TTT AAT AAT GTA ATA CCC
Trp Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro>



Fig.26B.

41/60

580	590	600	610	620
*	*	*	*	*
GAA GGT ATG AAC TTG AGT TTC CTC ATT GCC TTA ATT TCA AAT AAT GGA Glu Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly>				
630	640	650	660	670
*	*	*	*	*
AAT TAC ACA TGT GTT ACA TAT CCA GAA AAT GGA CGT ACG TTT CAT Asn Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His>				
680	690	700	710	720
*	*	*	*	*
CTC ACC AGG ACT CTG ACT GTA AAG GTA GTC TCT CCA AAA AAT GCA Leu Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala>				
730	740	750	760	
*	*	*	*	*
GTG CCC CCT GTG ATC CAT TCA CCT AAT GAT CAT GTG GTC TAT GAG AAA Val Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys>				
770	780	790	800	810
*	*	*	*	*
GAA CCA GGA GAG GAG CTA CTC ATT CCC TGT ACG GTC TAT TTT AGT TTT Glu Pro Gly Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe>				
820	830	840	850	860
*	*	*	*	*
CTG ATG GAT TCT CGC AAT GAG GTT TGG TGG ACC ATT GAT GGA AAA AAA Leu Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys>				
870	880	890	900	910
*	*	*	*	*
CCT GAT GAC ATC ACT ATT GAT GTC ACC ATT AAC GAA AGT ATA AGT CAT Pro Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His>				
920	930	940	950	960
*	*	*	*	*
AGT AGA ACA GAA GAT GAA ACA AGA ACT CAG ATT TTG AGC ATC AAG AAA Ser Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys>				
970	980	990	1000	
*	*	*	*	*
GTT ACC TCT GAG GAT CTC AAG CGC AGC TAT GTC TGT CAT GCT AGA AGT Val Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser>				
1010	1020	1030	1040	1050
*	*	*	*	*
GCC AAA GGC GAA GTT GCC AAA GCA GCC AAG GTG AAG CAG AAA GTG CCA Ala Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro>				
1060	1070	1080	1090	1100
*	*	*	*	*
GCT CCA AGA TAC ACA GTG TCC GGT GGC GCG CCT ATG CTG AGC GAG GCT Ala Pro Arg Tyr Thr Val Ser Gly Gly Ala Pro Met Leu Ser Glu Ala>				
1110	1120	1130	1140	1150
*	*	*	*	*
GAT AAA TGC AAG GAA CGT GAA GAA AAA ATA ATT TTA GTG TCA TCT GCA Asp Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile Leu Val Ser Ser Ala>				
1160	1170	1180	1190	1200
*	*	*	*	*

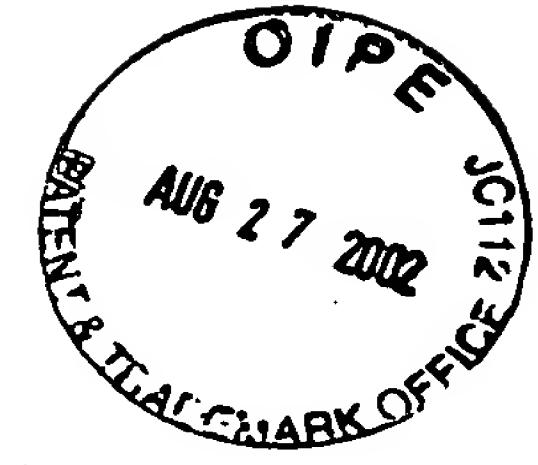


42/60

Fig.26C.

AAT GAA ATT GAT GTT CGT CCC TGT CCT CTT AAC CCA AAT GAA CAC AAA
Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn Pro Asn Glu His Lys>

1210 1220 1230 1240
* * * * * * * * * * * *
GGC ACT ATA ACT TGG TAT AAG GAT GAC AGC AAG ACA CCT GTA TCT ACA
Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys Thr Pro Val Ser Thr>
1250 1260 1270 1280 1290
* * * * * * * * * * * * * *
GAA CAA GCC TCC AGG ATT CAT CAA CAC AAA GAG AAA CTT TGG TTT GTT
Glu Gln Ala Ser Arg Ile His Gln His Lys Glu Lys Leu Trp Phe Val>
1300 1310 1320 1330 1340
* * * * * * * * * * * *
CCT GCT AAG GTG GAG GAT TCA GGA CAT TAC TAT TGC GTG GTA AGA AAT
Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr Cys Val Val Arg Asn>
1350 1360 1370 1380 1390
* * * * * * * * * * * *
TCA TCT TAC TGC CTC AGA ATT AAA ATA AGT GCA AAA TTT GTG GAG AAT
Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala Lys Phe Val Glu Asn>
1400 1410 1420 1430 1440
* * * * * * * * * * * *
GAG CCT AAC TTA TGT TAT AAT GCA CAA GCC ATA TTT AAG CAG AAA CTA
Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile Phe Lys Gln Lys Leu>
1450 1460 1470 1480
* * * * * * * * * * * *
CCC GTT GCA GGA GAC GGA GGA CTT GTG TGC CCT TAT ATG GAG TTT TTT
Pro Val Ala Gly Asp Gly Leu Val Cys Pro Tyr Met Glu Phe Phe>
1490 1500 1510 1520 1530
* * * * * * * * * * * *
AAA AAT GAA AAT AAT GAG TTA CCT AAA TTA CAG TGG TAT AAG GAT TGC
Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln Trp Tyr Lys Asp Cys>
1540 1550 1560 1570 1580
* * * * * * * * * * * *
AAA CCT CTA CTT CTT GAC AAT ATA CAC TTT AGT GGA GTC AAA GAT AGG
Lys Pro Leu Leu Asp Asn Ile His Phe Ser Gly Val Lys Asp Arg>
1590 1600 1610 1620 1630
* * * * * * * * * * * *
CTC ATC GTG ATG AAT GTG GCT GAA AAG CAT AGA GGG AAC TAT ACT TGT
Leu Ile Val Met Asn Val Ala Glu Lys His Arg Gly Asn Tyr Thr Cys>
1640 1650 1660 1670 1680
* * * * * * * * * * * *
CAT GCA TCC TAC ACA TAC TTG GGC AAG CAA TAT CCT ATT ACC CGG GTA
His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr Pro Ile Thr Arg Val>
1690 1700 1710 1720
* * * * * * * * * * * *
ATA GAA TTT ATT ACT CTA GAG GAA AAC AAA CCC ACA AGG CCT GTG ATT
Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro Thr Arg Pro Val Ile>
1730 1740 1750 1760 1770
* * * * * * * * * * * *
GTG AGC CCA GCT AAT GAG ACA ATG GAA GTA GAC TTG GGA TCC CAG ATA
Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp Leu Gly Ser Gln Ile>



43/60

Fig.26D.

1780	1790	1800	1810	1820
*	*	*	*	*
CAA TTG ATC TGT AAT GTC ACC GGC CAG TTG AGT GAC ATT GCT TAC TGG Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser Asp Ile Ala Tyr Trp>				
1830	1840	1850	1860	1870
*	*	*	*	*
AAG TGG AAT GGG TCA GTA ATT GAT GAA GAT GAC CCA GTG CTA GGG GAA Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp Pro Val Leu Gly Glu>				
1880	1890	1900	1910	1920
*	*	*	*	*
GAC TAT TAC AGT GTG GAA AAT CCT GCA AAC AAA AGA AGG AGT ACC CTC Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys Arg Arg Ser Thr Leu>				
1930	1940	1950	1960	
*	*	*	*	*
ATC ACA GTG CTT AAT ATA TCG GAA ATT GAG AGT AGA TTT TAT AAA CAT Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser Arg Phe Tyr Lys His>				
1970	1980	1990	2000	2010
*	*	*	*	*
CCA TTT ACC TGT TTT GCC AAG AAT ACA CAT GGT ATA GAT GCA GCA TAT Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly Ile Asp Ala Ala Tyr>				
2020	2030	2040	2050	2060
*	*	*	*	*
ATC CAG TTA ATA TAT CCA GTC ACT AAT TCC GGA GAC AAA ACT CAC ACA Ile Gln Leu Ile Tyr Pro Val Thr Asn Ser Gly Asp Lys Thr His Thr>				
2070	2080	2090	2100	2110
*	*	*	*	*
TGC CCA CCG TGC CCA GCA CCT GAA CTC CTG GGG GGA CCG TCA GTC TTC Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe>				
2120	2130	2140	2150	2160
*	*	*	*	*
CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC TCC CGG ACC CCT Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro>				
2170	2180	2190	2200	
*	*	*	*	*
GAG GTC ACA TGC GTG GTG GAC GTG AGC CAC GAA GAC CCT GAG GTC Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val>				
2210	2220	2230	2240	2250
*	*	*	*	*
AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT GCC AAG ACA Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr>				
2260	2270	2280	2290	2300
*	*	*	*	*
AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC GTC Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val>				
2310	2320	2330	2340	2350
*	*	*	*	*
CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys>				
2360	2370	2380	2390	2400



44/60

Fig.26E.



45/60

Fig.27.

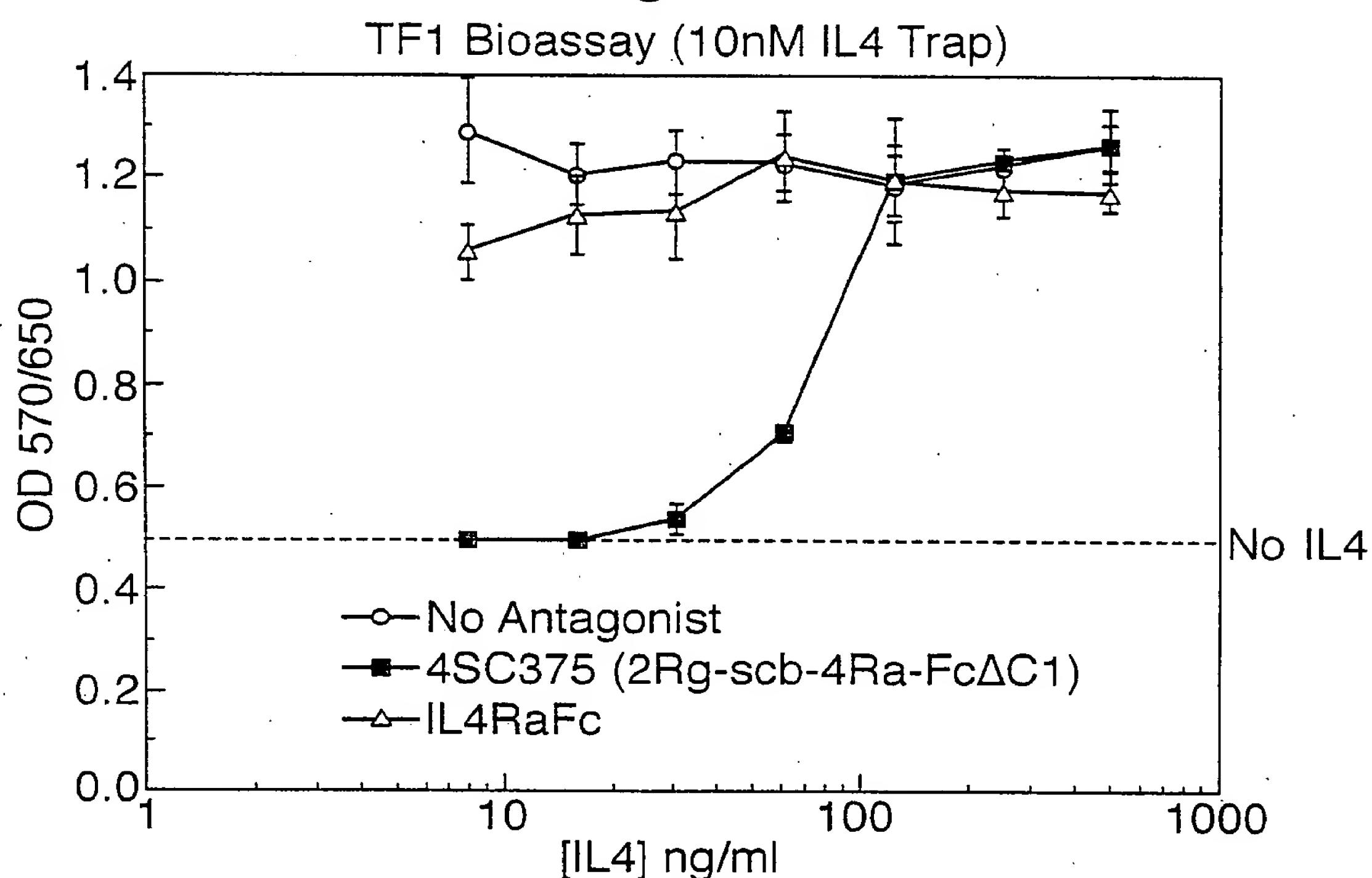
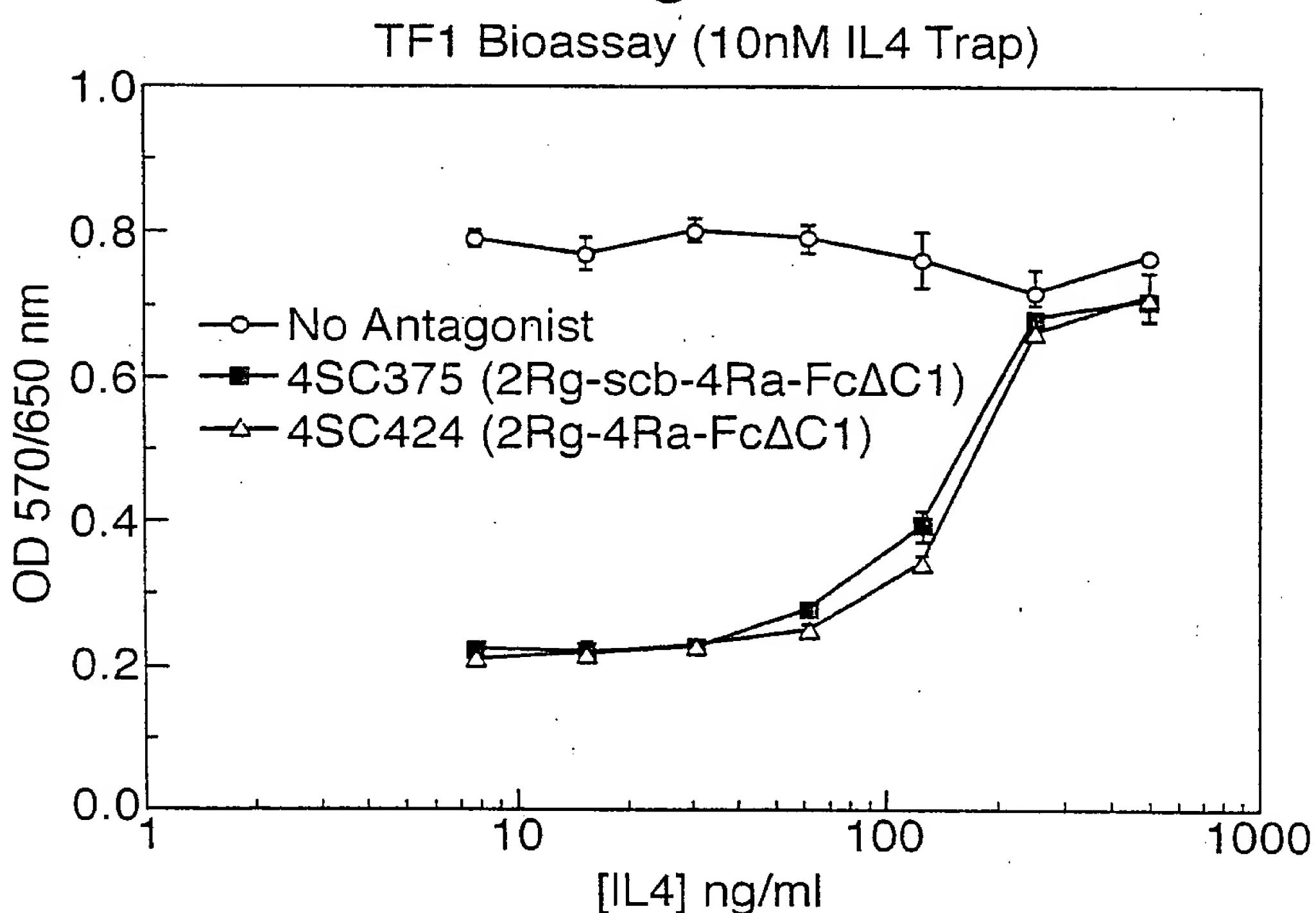


Fig.28.





46/60

Fig.29.

XG1 Bioassay (10nM IL6 Trap)

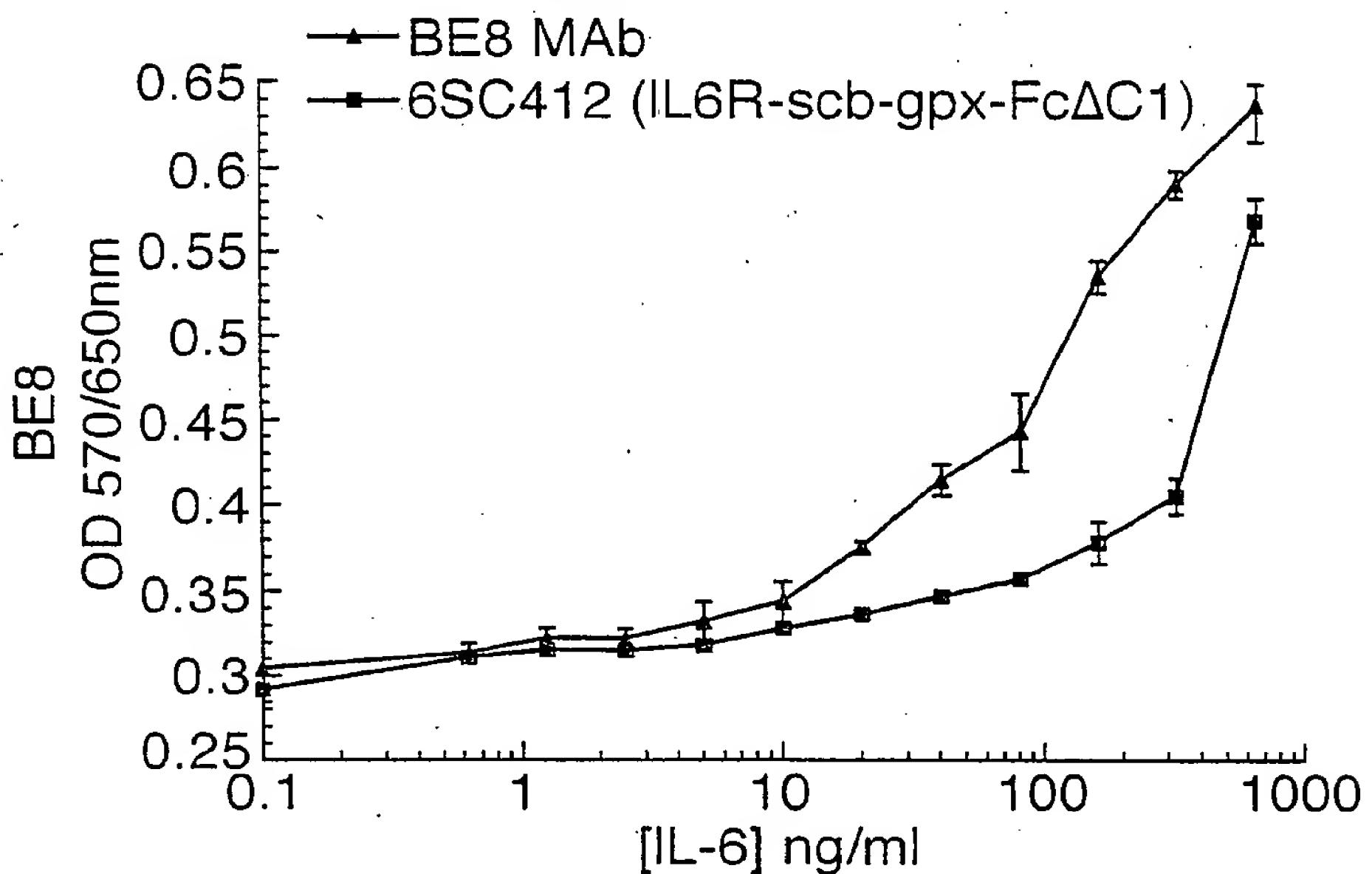
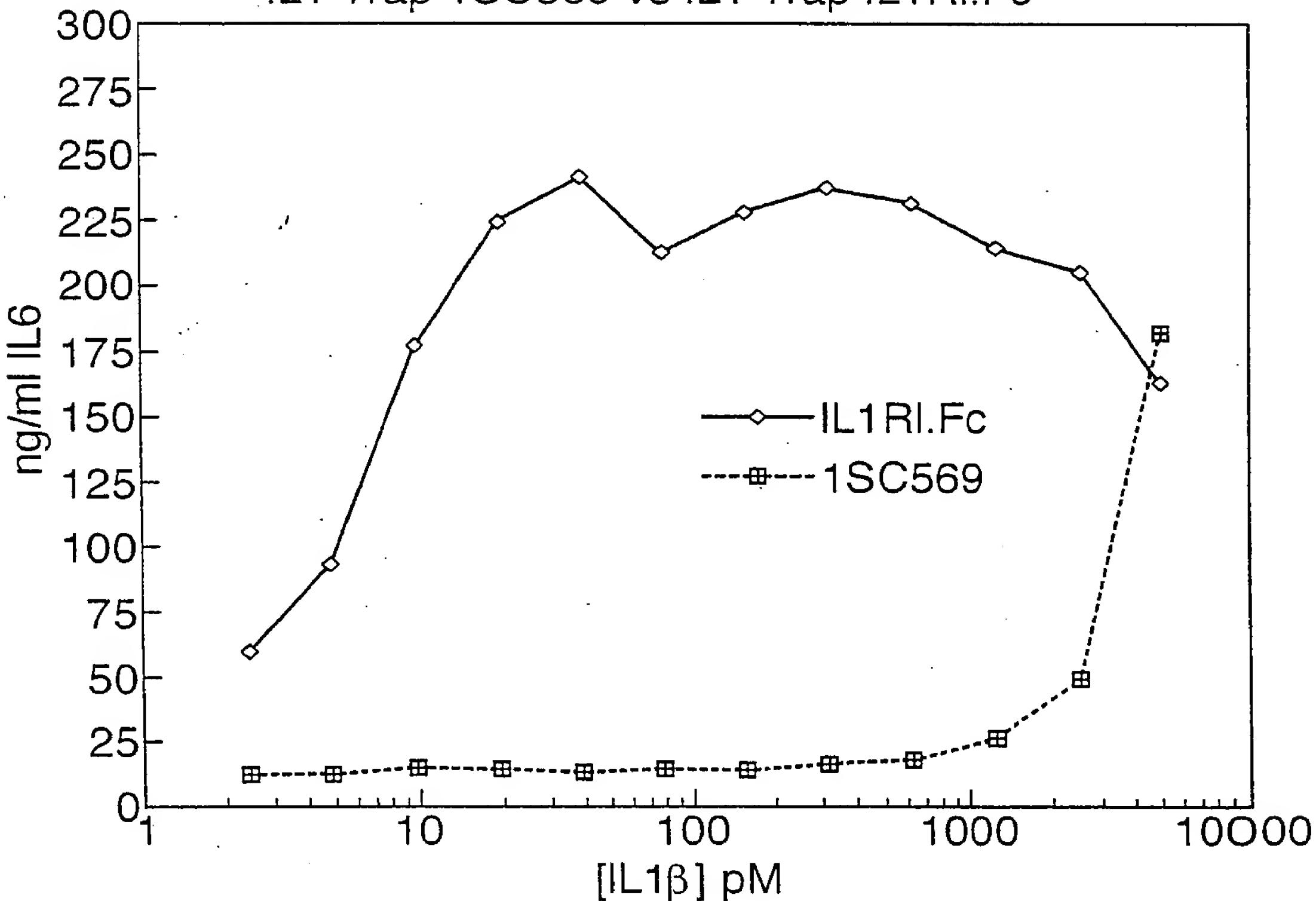


Fig.30.

MRC5 Bioassay (10nM IL1 Trap)

IL1 Trap 1SC569 vs IL1 Trap IL1RI.Fc





47/60

Fig.31A.

10 20 30 40
* * * * * * * * * * * * *
ATG GTG TGG CTT TGC TCT GGG CTC CTG TTC CCT GTG AGC TGC CTG GTC
TAC CAC ACC GAA ACG AGA CCC GAG GAC AAG GGA CAC TCG ACG GAC CAG
Met Val Trp Leu Cys Ser Gly Leu Leu Phe Pro Val Ser Cys Leu Val>

50 60 70 80 90
* * * * * * * * * * * * *
CTG CTG CAG GTG GCA AGC TCT GGG AAC ATG AAG GTC TTG CAG GAG CCC
GAC GAC GTC CAC CGT TCG AGA CCC TTG TAC TTC CAG AAC GTC CTC GGG
Leu Leu Gln Val Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro>

100 110 120 130 140
* * * * * * * * * * * * *
ACC TGC GTC TCC GAC TAC ATG AGC ATC TCT ACT TGC GAG TGG AAG ATG
TGG ACG CAG AGG CTG ATG TAC TCG TAG AGA TGA ACG CTC ACC TTC TAC
Thr Cys Val Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met>

150 160 170 180 190
* * * * * * * * * * * * *
AAT GGT CCC ACC AAT TGC AGC ACC GAG CTC CGC CTG TTG TAC CAG CTG
TTA CCA GGG TGG TTA ACG TCG TGG CTC GAG GCG GAC AAC ATG GTC GAC
Asn Gly Pro Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu>

200 210 220 230 240
* * * * * * * * * * * * *
GTT TTT CTG CTC TCC GAA GCC CAC ACG TGT ATC CCT GAG AAC AAC GGA
CAA AAA GAC GAG AGG CTT CGG GTG TGC ACA TAG GGA CTC TTG TTG CCT
Val Phe Leu Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly>

250 260 270 280
* * * * * * * * * * * * *
GGC GCG GGG TGC GTG TGC CAC CTG CTC ATG GAT GAC GTG GTC AGT GCG
CCG CGC CCC ACG CAC ACG GTG GAC GAG TAC CTA CTG CAC CAG TCA CGC
Gly Ala Gly Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala>

290 300 310 320 330
* * * * * * * * * * * * *
GAT AAC TAT ACA CTG GAC CTG TGG GCT GGG CAG CAG CTG CTG TGG AAG
CTA TTG ATA TGT GAC CTG GAC ACC CGA CCC GTC GTC GAC GAC ACC TTC
Asp Asn Tyr Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys>

340 350 360 370 380
* * * * * * * * * * * * *
GGC TCC TTC AAG CCC AGC GAG CAT GTG AAA CCC AGG GCC CCA GGA AAC
CCG AGG AAG TTC GGG TCG CTC GTA CAC TTT GGG TCC CGG GGT CCT TTG
Gly Ser Phe Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn>



48/60

Fig.31B.

390	400	410	420	430
* * *	* *	* *	* *	* *
CTG ACA GTT CAC ACC AAT GTC TCC GAC ACT CTG CTG CTG ACC TGG AGC				
GAC TGT CAA GTG TGG TTA CAG AGG CTG TGA GAC GAC GAC TGG ACC TCG				
Leu Thr Val His Thr Asn Val Ser Asp Thr Leu Leu Leu Thr Trp Ser>				
440	450	460	470	480
* *	* *	* *	* *	* *
AAC CCG TAT CCC CCT GAC AAT TAC CTG TAT AAT CAT CTC ACC TAT GCA				
TTG GGC ATA GGG GGA CTG TTA ATG GAC ATA TTA GTA GAG TGG ATA CGT				
Asn Pro Tyr Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala>				
490	500	510	520	
* *	* *	* *	* *	
GTC AAC ATT TGG AGT GAA AAC GAC CCG GCA GAT TTC AGA ATC TAT AAC				
CAG TTG TAA ACC TCA CTT TTG CTG GGC CGT CTA AAG TCT TAG ATA TTG				
Val Asn Ile Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn>				
530	540	550	560	570
* *	* *	* *	* *	* *
GTG ACC TAC CTA GAA CCC TCC CTC CGC ATC GCA GCC AGC ACC CTG AAG				
CAC TGG ATG GAT CTT GGG AGG GAG GCG TAG CGT CGG TCG TGG GAC TTC				
Val Thr Tyr Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys>				
580	590	600	610	620
* *	* *	* *	* *	* *
TCT GGG ATT TCC TAC AGG GCA CGG GTG AGG GCC TGG GCT CAG AGC TAT				
AGA CCC TAA AGG ATG TCC CGT GCC CAC TCC CGG ACC CGA GTC TCG ATA				
Ser Gly Ile Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Ser Tyr>				
630	640	650	660	670
* *	* *	* *	* *	* *
AAC ACC ACC TGG AGT GAG TGG AGC CCC AGC ACC AAG TGG CAC AAC TCC				
TTG TGG TGG ACC TCA CTC ACC TCG GGG TCG TGG TTC ACC GTG TTG AGG				
Asn Thr Thr Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser>				
680	690	700	710	720
* *	* *	* *	* *	* *
TAC AGG GAG CCC TTC GAG CAG TCC GGT GGG GGC GGG GGC GCC GCG CCT				
ATG TCC CTC GGG AAG CTC GTC AGG CCA CCC CCG CCC CCG CGG CGC GGA				
Tyr Arg Glu Pro Phe Glu Gln Ser Gly Gly Gly Gly Ala Ala Pro>				
730	740	750	760	
* *	* *	* *	* *	
ACG GAA ACT CAG CCA CCT GTG ACA AAT TTG AGT GTC TCT GTT GAA AAC				
TGC CTT TGA GTC GGT GGA CAC TGT TTA AAC TCA CAG AGA CAA CTT TTG				
Thr Glu Thr Gln Pro Pro Val Thr Asn Leu Ser Val Ser Val Glu Asn>				



49/60

Fig.31C.

770 780 790 800 810
* * * * * * *
CTC TGC ACA GTA ATA TGG ACA TGG AAT CCA CCC GAG GGA GCC AGC TCA
GAG ACG TGT CAT TAT ACC TGT ACC TTA GGT GGG CTC CCT CGG TCG AGT
Leu Cys Thr Val Ile Trp Thr Trp Asn Pro Pro Glu Gly Ala Ser Ser>

820 830 840 850 860
* * * * * * *
AAT TGT AGT CTA TGG TAT TTT AGT CAT TTT GGC GAC AAA CAA GAT AAG
TTA ACA TCA GAT ACC ATA AAA TCA GTA AAA CCG CTG TTT GTT CTA TTC
Asn Cys Ser Leu Trp Tyr Phe Ser His Phe Gly Asp Lys Gln Asp Lys>

870 880 890 900 910
* * * * * * *
AAA ATA GCT CCG GAA ACT CGT CGT TCA ATA GAA GTA CCC CTG AAT GAG
TTT TAT CGA GGC CTT TGA GCA GCA AGT TAT CTT CAT GGG GAC TTA CTC
Lys Ile Ala Pro Glu Thr Arg Arg Ser Ile Glu Val Pro Leu Asn Glu>

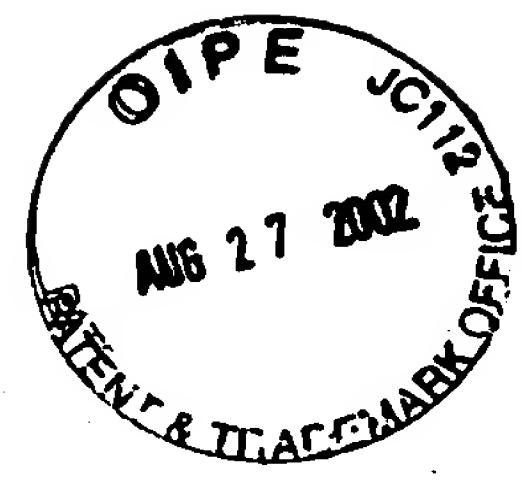
920 930 940 950 960
* * * * * * *
AGG ATT TGT CTG CAA GTG GGG TCC CAG TGT AGC ACC AAT GAG AGT GAG
TCC TAA ACA GAC GTT CAC CCC AGG GTC ACA TCG TGG TTA CTC TCA CTC
Arg Ile Cys Leu Gln Val Gly Ser Gln Cys Ser Thr Asn Glu Ser Glu>

970 980 990 1000
* * * * * * *
AAG CCT AGC ATT TTG GTT GAA AAA TGC ATC TCA CCC CCA GAA GGT GAT
TTC GGA TCG TAA AAC CAA CTT TTT ACG TAG AGT GGG GGT CTT CCA CTA
Lys Pro Ser Ile Leu Val Glu Lys Cys Ile Ser Pro Pro Glu Gly Asp>

1010 1020 1030 1040 1050
* * * * * * *
CCT GAG TCT GCT GTG ACT GAG CTT CAA TGC ATT TGG CAC AAC CTG AGC
GGA CTC AGA CGA CAC TGA CTC GAA GTT ACG TAA ACC GTG TTG GAC TCG
Pro Glu Ser Ala Val Thr Glu Leu Gln Cys Ile Trp His Asn Leu Ser>

1060 1070 1080 1090 1100
* * * * * * *
TAC ATG AAG TGT TCT TGG CTC CCT GGA AGG AAT ACC AGT CCC GAC ACT
ATG TAC TTC ACA AGA ACC GAG GGA CCT TCC TTA TGG TCA GGG CTG TGA
Tyr Met Lys Cys Ser Trp Leu Pro Gly Arg Asn Thr Ser Pro Asp Thr>

1110 1120 1130 1140 1150
* * * * * * *
AAC TAT ACT CTC TAC TAT TGG CAC AGA AGC CTG GAA AAA ATT CAT CAA
TTG ATA TGA GAG ATG ATA ACC GTG TCT TCG GAC CTT TTT TAA GTA GTT
Asn Tyr Thr Leu Tyr Tyr Trp His Arg Ser Leu Glu Lys Ile His Gln>



50/60

Fig.31D.

1160	1170	1180	1190	1200
*	*	*	*	*
TGT GAA AAC ATC TTT AGA GAA GGC CAA TAC TTT GGT TGT TCC TTT GAT				
ACA CTT TTG TAG AAA TCT CTT CCG GTT ATG AAA CCA ACA AGG AAA CTA				
Cys Glu Asn Ile Phe Arg Glu Gly Gln Tyr Phe Gly Cys Ser Phe Asp>				
1210	1220	1230	1240	
*	*	*	*	*
CTG ACC AAA GTG AAG GAT TCC AGT TTT GAA CAA CAC AGT GTC CAA ATA				
GAC TGG TTT CAC TTC CTA AGG TCA AAA CTT GTT GTG TCA CAG GTT TAT				
Leu Thr Lys Val Lys Asp Ser Ser Phe Glu Gln His Ser Val Gln Ile>				
1250	1260	1270	1280	1290
*	*	*	*	*
ATG GTC AAG GAT AAT GCA GGA AAA ATT AAA CCA TCC TTC AAT ATA GTG				
TAC CAG TTC CTA TTA CGT CCT TTT TAA TTT GGT AGG AAG TTA TAT CAC				
Met Val Lys Asp Asn Ala Gly Lys Ile Lys Pro Ser Phe Asn Ile Val>				
1300	1310	1320	1330	1340
*	*	*	*	*
CCT TTA ACT TCC CGT GTG AAA CCT GAT CCT CCA CAT ATT AAA AAC CTC				
GGA AAT TGA AGG GCA CAC TTT GGA CTA GGA GGT GTA TAA TTT TTG GAG				
Pro Leu Thr Ser Arg Val Lys Pro Asp Pro Pro His Ile Lys Asn Leu>				
1350	1360	1370	1380	1390
*	*	*	*	*
TCC TTC CAC AAT GAT GAC CTA TAT GTG CAA TGG GAG AAT CCA CAG AAT				
AGG AAG GTG TTA CTA CTG GAT ATA CAC GTT ACC CTC TTA GGT GTC TTA				
Ser Phe His Asn Asp Asp Leu Tyr Val Gln Trp Glu Asn Pro Gln Asn>				
1400	1410	1420	1430	1440
*	*	*	*	*
TTT ATT AGC AGA TGC CTA TTT TAT GAA GTA GAA GTC AAT AAC AGC CAA				
AAA TAA TCG TCT ACG GAT AAA ATA CTT CAT CTT CAG TTA TTG TCG GTT				
Phe Ile Ser Arg Cys Leu Phe Tyr Glu Val Glu Val Asn Asn Ser Gln>				
1450	1460	1470	1480	
*	*	*	*	*
ACT GAG ACA CAT AAT GTT TTC TAC GTC CAA GAG GCT AAA TGT GAG AAT				
TGA CTC TGT GTA TTA CAA AAG ATG CAG GTT CTC CGA TTT ACA CTC TTA				
Thr Glu Thr His Asn Val Phe Tyr Val Gln Glu Ala Lys Cys Glu Asn>				
1490	1500	1510	1520	1530
*	*	*	*	*
CCA GAA TTT GAG AGA AAT GTG GAG AAT ACA TCT TGT TTC ATG GTC CCT				
GGT CTT AAA CTC TCT TTA CAC CTC TTA TGT AGA ACA AAG TAC CAG GGA				
Pro Glu Phe Glu Arg Asn Val Glu Asn Thr Ser Cys Phe Met Val Pro>				



51/60

Fig.31E.

1540	1550	1560	1570	1580
*	*	*	*	*
GGT GTT CTT CCT GAT ACT TTG AAC ACA GTC AGA ATA AGA GTC AAA ACA				
CCA CAA GAA GGA CTA TGA AAC TTG TGT CAG TCT TAT TCT CAG TTT TGT				
Gly Val Leu Pro Asp Thr Leu Asn Thr Val Arg Ile Arg Val Lys Thr>				
1590	1600	1610	1620	1630
*	*	*	*	*
AAT AAG TTA TGC TAT GAG GAT GAC AAA CTC TGG AGT AAT TGG AGC CAA				
TTA TTC AAT ACG ATA CTC CTA CTG TTT GAG ACC TCA TTA ACC TCG GTT				
Asn Lys Leu Cys Tyr Glu Asp Asp Lys Leu Trp Ser Asn Trp Ser Gln>				
1640	1650	1660	1670	1680
*	*	*	*	*
GAA ATG AGT ATA GGT AAG AAG CGC AAT TCC ACA ACC GGA GAC AAA ACT				
CTT TAC TCA TAT CCA TTC TGC GCG TTA AGG TGT TGG CCT CTG TTT TGA				
Glu Met Ser Ile Gly Lys Lys Arg Asn Ser Thr Thr Gly Asp Lys Thr>				
1690	1700	1710	1720	
*	*	*	*	
CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA CTC CTG GGG GGA CCG TCA				
GTG TGT ACG GGT GGC ACG GGT CGT GGA CTT GAG GAC CCC CCT GGC AGT				
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser>				
1730	1740	1750	1760	1770
*	*	*	*	*
GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC TCC CGG				
CAG AAG GAG AAG GGG GGT TTT GGG TTC CTG TGG GAG TAC TAG AGG GCC				
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg>				
1780	1790	1800	1810	1820
*	*	*	*	*
ACC CCT GAG GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC CCT				
TGG GGA CTC CAG TGT ACG CAC CAC CAC CTG CAC TCG GTG CTT CTG GGA				
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro>				
1830	1840	1850	1860	1870
*	*	*	*	*
GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT GCC				
CTC CAG TTC AAG TTG ACC ATG CAC CTG CCG CAC CTC CAC GTA TTA CGG				
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala>				
1880	1890	1900	1910	1920
*	*	*	*	*
AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC				
TTC TGT TTC GGC GCC CTC CTC GTC ATG TTG TCG TGC ATG GCA CAC CAG				
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val>				



52/60

Fig.31F.

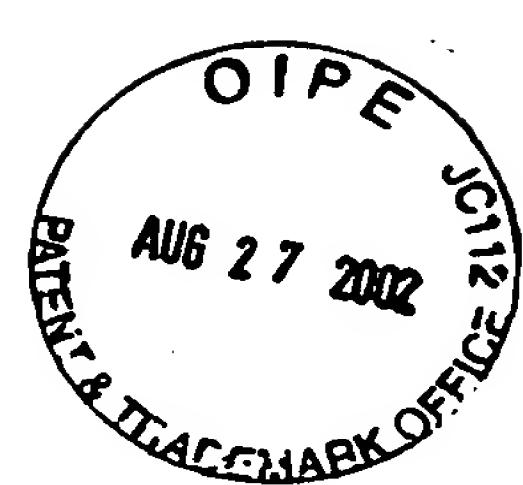
1930	1940	1950	1960	
*	*	*	*	*
AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC	TCG CAG GAG TGG CAG GAC GTG GTC CTG ACC GAC TTA CCG TTC CTC ATG	Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr>		
1970	1980	1990	2000	2010
*	*	*	*	*
AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC	TTC ACG TTC CAG AGG TTG TTT CGG GAG GGT CGG GGG TAG CTC TTT TGG	Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr>		
2020	2030	2040	2050	2060
*	*	*	*	*
ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG	TAG AGG TTT CGG TTT CCC GTC GGG GCT CTT GGT GTC CAC ATG TGG GAC	Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu>		
2070	2080	2090	2100	2110
*	*	*	*	*
CCC CCA TCC CGG GAG GAG ATG ACC AAG AAC CAG GTC AGC CTG ACC TGC	GGG GGT AGG GCC CTC CTC TAC TGG TTC TTG GTC CAG TCG GAC TGG ACG	Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys>		
2120	2130	2140	2150	2160
*	*	*	*	*
CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC	GAC CAG TTT CCG AAG ATA GGG TCG CTG TAG CGG CAC CTC ACC CTC TCG	Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser>		
2170	2180	2190	2200	
*	*	*	*	
AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG GAC	TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA GGG CAC GAC CTG	Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp>		
2210	2220	2230	2240	2250
*	*	*	*	*
TCC GAC GGC TCC TTC TTC CTC TAT AGC AAG CTC ACC GTG GAC AAG AGC	AGG CTG CCG AGG AAG AAG GAG ATA TCG TTC GAG TGG CAC CTG TTC TCG	Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser>		
2260	2270	2280	2290	2300
*	*	*	*	*
AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT	TCC ACC GTC GTC CCC TTG CAG AAG AGT ACG AGG CAC TAC GTA CTC CGA	Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala>		

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et al.
USSN: 09/313,942
Docket No.: REG 203-A



53/60

Fig.31G.



54/60

Fig.32A.

10 20 30 40
* * * * * *
ATG GTG TGG CCG GCG CGG CTC TGC GGG CTG TGG GCG CTG CTG CTC TGC
TAC CAC ACC GGC CGC GCC GAG ACG CCC GAC ACC CGC GAC GAC GAG ACG
Met Val Trp Pro Ala Arg Leu Cys Gly Leu Trp Ala Leu Leu Leu Cys>

50 60 70 80 90
* * * * * *
GCC GGC GGC GGG GGC GGG GGC GGG GGC GCC GCG CCT ACG GAA ACT CAG
CGG CCG CCG CCC CCG CCC CCG CCG CGC GGA TGC CTT TGA GTC
Ala Gly Gly Gly Gly Gly Ala Ala Pro Thr Glu Thr Gln>

100 110 120 130 140
* * * * * *
CCA CCT GTG ACA AAT TTG AGT GTC TCT GTT GAA AAC CTC TGC ACA GTA
GGT GGA CAC TGT TTA AAC TCA CAG AGA CAA CTT TTG GAG ACG TGT CAT
Pro Pro Val Thr Asn Leu Ser Val Ser Val Glu Asn Leu Cys Thr Val>

150 160 170 180 190
* * * * * *
ATA TGG ACA TGG AAT CCA CCC GAG GGA GCC AGC TCA AAT TGT AGT CTA
TAT ACC TGT ACC TTA GGT GGG CTC CCT CGG TCG AGT TTA ACA TCA GAT
Ile Trp Thr Trp Asn Pro Pro Glu Gly Ala Ser Ser Asn Cys Ser Leu>

200 210 220 230 240
* * * * * *
TGG TAT TTT AGT CAT TTT GGC GAC AAA CAA GAT AAG AAA ATA GCT CCG
ACC ATA AAA TCA GTA AAA CCG CTG TTT GTT CTA TTC TTT TAT CGA GGC
Trp Tyr Phe Ser His Phe Gly Asp Lys Gln Asp Lys Lys Ile Ala Pro>

250 260 270 280
* * * * * *
GAA ACT CGT CGT TCA ATA GAA GTA CCC CTG AAT GAG AGG ATT TGT CTG
CTT TGA GCA GCA AGT TAT CTT CAT GGG GAC TTA CTC TCC TAA ACA GAC
Glu Thr Arg Arg Ser Ile Glu Val Pro Leu Asn Glu Arg Ile Cys Leu>

290 300 310 320 330
* * * * * *
CAA GTG GGG TCC CAG TGT AGC ACC AAT GAG AGT GAG AAG CCT AGC ATT
GTT CAC CCC AGG GTC ACA TCG TGG TTA CTC TCA CTC TTC GGA TCG TAA
Gln Val Gly Ser Gln Cys Ser Thr Asn Glu Ser Glu Lys Pro Ser Ile>

340 350 360 370 380
* * * * * *
TTG GTT GAA AAA TGC ATC TCA CCC CCA GAA GGT GAT CCT GAG TCT GCT
AAC CAA CTT TTT ACG TAG AGT GGG GGT CTT CCA CTA GGA CTC AGA CGA
Leu Val Glu Lys Cys Ile Ser Pro Pro Glu Gly Asp Pro Glu Ser Ala>



55/60

Fig. 32B.

390	400	410	420	430
*	*	*	*	*
GTG ACT GAG CTT CAA TGC ATT TGG CAC AAC CTG AGC TAC ATG AAG TGT	CAC TGA CTC GAA GTT ACG TAA ACC GTG TTG GAC TCG ATG TAC TTC ACA	Val Thr Glu Leu Gln Cys Ile Trp His Asn Leu Ser Tyr Met Lys Cys>		
440	450	460	470	480
*	*	*	*	*
TCT TGG CTC CCT GGA AGG AAT ACC AGT CCC GAC ACT AAC TAT ACT CTC	AGA ACC GAG GGA CCT TCC TTA TGG TCA GGG CTG TGA TTG ATA TGA GAG	Ser Trp Leu Pro Gly Arg Asn Thr Ser Pro Asp Thr Asn Tyr Thr Leu>		
490	500	510	520	
*	*	*	*	*
TAC TAT TGG CAC AGA AGC CTG GAA AAA ATT CAT CAA TGT GAA AAC ATC	ATG ATA ACC GTG TCT TCG GAC CTT TTT TAA GTA GTT ACA CTT TTG TAG	Tyr Tyr Trp His Arg Ser Leu Glu Lys Ile His Gln Cys Glu Asn Ile>		
530	540	550	560	570
*	*	*	*	*
TTT AGA GAA GGC CAA TAC TTT GGT TGT TCC TTT GAT CTG ACC AAA GTG	AAA TCT CTT CCG GTT ATG AAA CCA ACA AGG AAA CTA GAC TGG TTT CAC	Phe Arg Glu Gly Gln Tyr Phe Gly Cys Ser Phe Asp Leu Thr Lys Val>		
580	590	600	610	620
*	*	*	*	*
AAG GAT TCC AGT TTT GAA CAA CAC AGT GTC CAA ATA ATG GTC AAG GAT	TTC CTA AGG TCA AAA CTT GTT GTG TCA CAG GTT TAT TAC CAG TTC CTA	Lys Asp Ser Ser Phe Glu Gln His Ser Val Gln Ile Met Val Lys Asp>		
630	640	650	660	670
*	*	*	*	*
AAT GCA GGA AAA ATT AAA CCA TCC TTC AAT ATA GTG CCT TTA ACT TCC	TTA CGT CCT TTT TAA TTT GGT AGG AAG TTA TAT CAC GGA AAT TGA AGG	Asn Ala Gly Lys Ile Lys Pro Ser Phe Asn Ile Val Pro Leu Thr Ser>		
680	690	700	710	720
*	*	*	*	*
CGT GTG AAA CCT GAT CCT CCA CAT ATT AAA AAC CTC TCC TTC CAC AAT	GCA CAC TTT GGA CTA GGA GGT GTA TAA TTT TTG GAG AGG AAG GTG TTA	Arg Val Lys Pro Asp Pro Pro His Ile Lys Asn Leu Ser Phe His Asn>		
730	740	750	760	
*	*	*	*	*
GAT GAC CTA TAT GTG CAA TGG GAG AAT CCA CAG AAT TTT ATT AGC AGA	CTA CTG GAT ATA CAC GTT ACC CTC TTA GGT GTC TTA AAA TAA TCG TCT	Asp Asp Leu Tyr Val Gln Trp Glu Asn Pro Gln Asn Phe Ile Ser Arg>		



56/60

Fig.32C.

770 780 790 800 810
* * * * * *
TGC CTA TTT TAT GAA GTA GAA GTC AAT AAC AGC CAA ACT GAG ACA CAT
ACG GAT AAA ATA CTT CAT CTT CAG TTA TTG TCG GTT TGA CTC TGT GTA
Cys Leu Phe Tyr Glu Val Glu Val Asn Asn Ser Gln Thr Glu Thr His>

820 830 840 850 860
* * * * * *
AAT GTT TTC TAC GTC CAA GAG GCT AAA TGT GAG AAT CCA GAA TTT GAG
TTA CAA AAG ATG CAG GTT CTC CGA TTT ACA CTC TTA GGT CTT AAA CTC
Asn Val Phe Tyr Val Gln Glu Ala Lys Cys Glu Asn Pro Glu Phe Glu>

870 880 890 900 910
* * * * * *
AGA AAT GTG GAG AAT ACA TCT TGT TTC ATG GTC CCT GGT GTT CTT CCT
TCT TTA CAC CTC TTA TGT AGA ACA AAG TAC CAG GGA CCA CAA GAA GGA
Arg Asn Val Glu Asn Thr Ser Cys Phe Met Val Pro Gly Val Leu Pro>

920 930 940 950 960
* * * * * *
GAT ACT TTG AAC ACA GTC AGA ATA AGA GTC AAA ACA AAT AAG TTA TGC
CTA TGA AAC TTG TGT CAG TCT TAT TCT CAG TTT TGT TTA TTC AAT ACG
Asp Thr Leu Asn Thr Val Arg Ile Arg Val Lys Thr Asn Lys Leu Cys>

970 980 990 1000
* * * * * *
TAT GAG GAT GAC AAA CTC TGG AGT AAT TGG AGC CAA GAA ATG AGT ATA
ATA CTC CTA CTG TTT GAG ACC TCA TTA ACC TCG GTT CTT TAC TCA TAT
Tyr Glu Asp Asp Lys Leu Trp Ser Asn Trp Ser Gln Glu Met Ser Ile>

1010 1020 1030 1040 1050
* * * * * *
GGT AAG AAG CGC AAT TCC ACA GGC GCG CCT AGT GGT GGA GGT GGC CGG
CCA TTC TTC GCG TTA AGG TGT CCG CGC GGA TCA CCA CCT CCA CCG GCC
Gly Lys Lys Arg Asn Ser Thr Gly Ala Pro Ser Gly Gly Gly Arg>

1060 1070 1080 1090 1100
* * * * * *
CCC GCA AGC TCT GGG AAC ATG AAG GTC TTG CAG GAG CCC ACC TGC GTC
GGG CGT TCG AGA CCC TTG TAC TTC CAG AAC GTC CTC GGG TGG ACG CAG
Pro Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro Thr Cys Val>

1110 1120 1130 1140 1150
* * * * * *
TCC GAC TAC ATG AGC ATC TCT ACT TGC GAG TGG AAG ATG AAT GGT CCC
AGG CTG ATG TAC TCG TAG AGA TGA ACG CTC ACC TTC TAC TTA CCA GGG
Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met Asn Gly Pro>



57/60

Fig.32D.

1160 1170 1180 1190 1200
* * * * * * *
ACC AAT TGC AGC ACC GAG CTC CGC CTG TTG TAC CAG CTG GTT TTT CTG
TGG TTA ACG TCG TGG CTC GAG GCG GAC AAC ATG GTC GAC CAA AAA GAC
Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu Val Phe Leu>

1210 1220 1230 1240
* * * * * * * *
CTC TCC GAA GCC CAC ACG TGT ATC CCT GAG AAC AAC GGA GGC GCG GGG
GAG AGG CTT CGG GTG TGC ACA TAG GGA CTC TTG TTG CCT CCG CGC CCC
Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly Gly Ala Gly>

1250 1260 1270 1280 1290
* * * * * * * * *
TGC GTG TGC CAC CTG CTC ATG GAT GAC GTG GTC AGT GCG GAT AAC TAT
ACG CAC ACG GTG GAC GAG TAC CTA CTG CAC CAG TCA CGC CTA TTG ATA
Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala Asp Asn Tyr>

1300 1310 1320 1330 1340
* * * * * * * * *
ACA CTG GAC CTG TGG GCT GGG CAG CAG CTG CTG TGG AAG GGC TCC TTC
TGT GAC CTG GAC ACC CGA CCC GTC GTC GAC GAC ACC TTC CCG AGG AAG
Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys Gly Ser Phe>

1350 1360 1370 1380 1390
* * * * * * * * *
AAG CCC AGC GAG CAT GTG AAA CCC AGG GCC CCA GGA AAC CTG ACA GTT
TTC GGG TCG CTC GTA CAC TTT GGG TCC CGG GGT CCT TTG GAC TGT CAA
Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn Leu Thr Val>

1400 1410 1420 1430 1440
* * * * * * * * *
CAC ACC AAT GTC TCC GAC ACT CTG CTG CTG ACC TGG AGC AAC CCG TAT
GTG TGG TTA CAG AGG CTG TGÀ GAC GAC GAC TGG ACC TCG TTG GGC ATA
His Thr Asn Val Ser Asp Thr Leu Leu Thr Trp Ser Asn Pro Tyr>

1450 1460 1470 1480
* * * * * * * * *
CCC CCT GAC AAT TAC CTG TAT AAT CAT CTC ACC TAT GCA GTC AAC ATT
GGG GGA CTG TTA ATG GAC ATA TTA GTA GAG TGG ATA CGT CAG TTG TAA
Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala Val Asn Ile>

1490 1500 1510 1520 1530
* * * * * * * * *
TGG AGT GAA AAC GAC CCG GCA GAT TTC AGA ATC TAT AAC GTG ACC TAC
ACC TCA CTT TTG CTG GGC CGT CTA AAG TCT TAG ATA TTG CAC TGG ATG
Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn Val Thr Tyr>



58/60

Fig.32E.

1540 1550 1560 1570 1580
*
CTA GAA CCC TCC CTC CGC ATC GCA GCC AGC ACC CTG AAG TCT GGG ATT
GAT CTT GGG AGG GAG GCG TAG CGT CGG TCG TGG GAC TTC AGA CCC TAA
Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys Ser Gly Ile>

1590 1600 1610 1620 1630
*
TCC TAC AGG GCA CGG GTG AGG GCC TGG GCT CAG TGC TAT AAC ACC ACC
AGG ATG TCC CGT GCC CAC TCC CGG ACC CGA GTC ACG ATA TTG TGG TGG
Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Cys Tyr Asn Thr Thr>

1640 1650 1660 1670 1680
*
TGG AGT GAG TGG AGC CCC AGC ACC AAG TGG CAC AAC TCC TAC AGG GAG
ACC TCA CTC ACC TCG GGG TCG TGG TTC ACC GTG TTG AGG ATG TCC CTC
Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser Tyr Arg Glu>

1690 1700 1710 1720
*
CCC TTC GAG CAG TCC GGA GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA
GGG AAG CTC GTC AGG CCT CTG TTT TGA GTG TGT ACG GGT GGC ACG GGT
Pro Phe Glu Gln Ser Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro>

1730 1740 1750 1760 1770
*
GCA CCT GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA
CGT GGA CTT GAG GAC CCC CCT GGC AGT CAG AAG GAG AAG GGG GGT TTT
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys>

1780 1790 1800 1810 1820
*
CCC AAG GAC ACC CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA TGC GTG
GGG TTC CTG TGG GAG TAC TAG AGG GCC TGG GGA CTC CAG TGT ACG CAC
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val>

1830 1840 1850 1860 1870
*
GTG GTG GAC GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC
CAC CAC CTG CAC TCG GTG CTT CTG GGA CTC CAG TTC AAG TTG ACC ATG
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr>

1880 1890 1900 1910 1920
*
GTG GAC GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG GAG
CAC CTG CCG CAC CTC CAC GTA TTA CGG TTC TGT GGC GCC CTC CTC
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu>

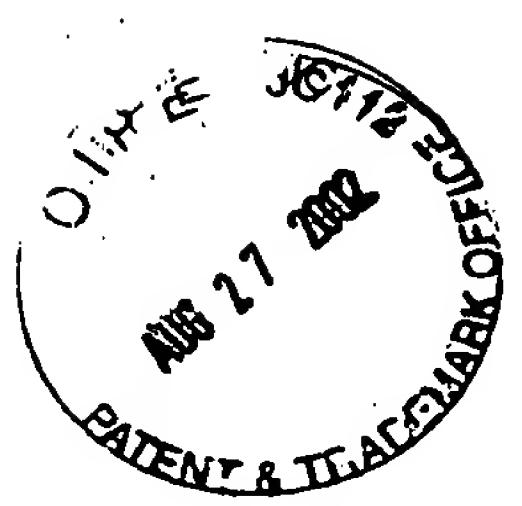


59/60

Fig.32F.

1930	1940	1950	1960	
*	*	*	*	*
CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC	GTC ATG TTG TCG TGC ATG GCA CAC CAG TCG CAG GAG TGG CAG GAC GTG	Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His>		
1970	1980	1990	2000	2010
*	*	*	*	*
CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA	GTC CTG ACC GAC TTA CCG TTC CTC ATG TTC ACG TTC CAG AGG TTG TTT	Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys>		
2020	2030	2040	2050	2060
*	*	*	*	*
GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG	CGG GAG GGT CGG GGG TAG CTC TTT TGG TAG AGG TTT CGG TTT CCC GTC	Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln>		
2070	2080	2090	2100	2110
*	*	*	*	*
CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAG GAG ATG	GGG GCT CTT GGT GTC CAC ATG TGG GAC GGG GGT AGG GCC CTC CTC TAC	Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met>		
2120	2130	2140	2150	2160
*	*	*	*	*
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC	TGG TTC TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT CCG AAG ATA GGG	Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro>		
2170	2180	2190	2200	
*	*	*	*	
AGC GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC	TCG CTG TAG CGG CAC CTC ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG	Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn>		
2210	2220	2230	2240	2250
*	*	*	*	*
TAC AAG ACC ACG CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC	ATG TTC TGG TGC GGA GGG CAC GAC CTG AGG CTG CCG AGG AAG AAG GAG	Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu>		
2260	2270	2280	2290	2300
*	*	*	*	*
TAT AGC AAG CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC	ATA TCG TTC GAG TGG CAC CTG TTC TCG TCC ACC GTC GTC CCC TTG CAG	Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val>		

Title: RECEPTOR BASED ANTAGONISTS
AND METHODS OF MAKING AND USING
INVENTOR: STAHL, et.al.
USSN: 09/313,942
Docket No.: REG 203-A



60/60

Fig.32G.

2310

2320

2330

2340

2350

* * * * *
TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG
AAG AGT ACG AGG CAC TAC GTA CTC CGA GAC GTG TTG GTG ATG TGC GTC
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln>

2360

2370

2380

* * * * *
AAG AGC CTC TCC CTG TCT CCG GGT AAA TGA
TTC TCG GAG AGG GAC AGA GGC CCA TTT ACT
Lys Ser Leu Ser Leu Ser Pro Gly Lys ***>